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EDITORIAL.

The Discussion Group.

"Reading Maketh a Full Man; Conference a Ready Man; and Writing an Exact Man."

All medical students know from experience what an excellent hypnotic it is to sit down and read a textbook's dogmatic, bald statements. We know also how much a subject gains in interest when a clinician or lecturer gives us an inkling of recent advances in a field or intimates that there is some doubt as to how a certain change takes place, or when the reading of an article, say, enables us to visualize the sequence of events in the development of a condition. These are the points that stick with us, and the reason is obvious—our interest is aroused.

A method of having our interest in this direction stimulated more frequently and thoroughly is by taking part in a discussion group. In preparing a paper or in hearing one read, we find what a live growing body of knowledge it is with which we are dealing—a very different picture from the valley of dry bones presented by the textbooks.

To mention very briefly some of the more obvious advantages of being a member of such a group: The practice in discovering and appraising knowledge is of inestimable value.

Very few of us are able by ourselves to overcome our starting inertia and to read beyond our textbooks and lecture notes; but with the stimulus of a group of fellow students many of us would do so. Again, we haven't the time to dig deeply into more than a very few subjects; in such a group, however, a considerable variety of subjects may be covered very effectively throughout the year.

Not the least important of the benefits that accrue from taking part in a discussion group are those that we will feel chiefly after graduation. The habit of reading current medical literature is one that will stick and will save us from "the killing vice of the young doctor, intellectual laziness."

The experience in discussion groups in preparing,, presenting and defending papers will stand many of us in good stead in after years in fulfilling a similar function at association meetings and in journals. Edinburgh has produced many famous speakers and writers on medical subjects, and credit is given there to the discussion groups which have been in existence for years.

It has been suggested that the Medical Society here should concern itself with the establishment of groups for the reading and discussion of papers on medical subjects. However, it is our opinion that success is more likely to be assured such groups if their formation is spontaneous. In this way the group will be congenial; initiative and discipline will be self-contained; and there will be freedom of direction and discussion.

A few practical suggestions on the conduct of such a group may be in order. The group should not be too large, certainly not over twenty in number, twelve is much preferable—for the sake of informality and freedom of discussion. The meetings should be frequent, at least fortnightly. It is well to invite one or two staff members to each meeting to assist in the discussion. As a diversion, an occasional meeting may be given over to an outstanding character in medical history. In this connection, Cushing in his "Life of Sir William Osler" presents a very attractive picture of the Saturday nights at Osler's house in Baltimore where a group of a dozen or so students would gather around the dining-room table while Osler himself or one of the students gave a paper on some ancient medical worthy, which was then discussed over beer and crackers and cheese.

We make no apology for introducing the subject of discussion groups at this time of the year. Our hope is that the seed sown now will bear fruit in the Fall. We should like it to take root in the minds of the members of the junior years particularly. Several discussion groups should be formed in each year. The Journal will be pleased to publish for the benefit of all of us the pre-eminent papers that are presented in such groups.

Differences in the Physiological Antagonisms of Ions.*

By ALBRECHT BETHE, M.D., Ph.D.
Frankfort on Main

The mineral analysis of the blood of different species of animals revealed the surprising fact that the quantitative relations of the constituent ions paralleled almost exactly the relation in sea water.

Just as in sea water, no matter whence it comes or how concentrated it may be, the ratios of Na to Ca, K and Mg are always the same, so too in the body fluids (juices) of animals the same approximate ratio between Na, Ca and K is found. Only with Mg are considerable variations in ratio to be found. I do not know who first referred to this similarity of relationship between the ions. But certainly Macallum and Quinton first laid stress upon it.

This fact would not be so surpris-

*This is the second of two papers by Albrecht Bethe, M.D., Ph.D. The first appeared in the March issue of this Journal. Translation is by Dr. V. E. Henderson and Dr. Bethe.

ing in the case of animals living constantly in sea water. But it is very striking in the case of animals living in the air, which though they are certainly descended from marine animals, nevertheless have now nothing to do with the sea. Perhaps it is still more astonishing in the case of animals living in fresh water in which the relation of the ions referred to often differs markedly from that prevailing in sea water.

There are lakes and rivers which contain very little Na and Cl but contain much Ca or Mg. In spite of this, Na and Cl are abundant in the blood of animals living in such water while the Ca and Mg content is low.

The juices of the lower marine animals reproduces almost exactly the relation between the ions of sea water. In higher marine animals (crustaceans) Mg is already decreasing and shows in the different species very varying values. But one never finds so low Mg values as are contained in the blood of the vertebrates. On the other hand, the Ca content is in most cases higher than in sea water, and the K content rises as the Mg decreases.

This shows that the body fluids of every species of animals under normal circumstances have a more or less specific ionic composition. If now, as I showed in a previous paper, the surfaces of most marine animals are permeable to salts, they must possess the ability to change the relations of the ions from that of sea water. But a real regulating mechanism—such as most vertebrates possess—obviously does not exist. The vertebrates are enabled to hold the relation of the ions constant in spite of the salts taken with food and drink, by the aid of their kidneys. But in marine circumstances or in molluscs, if you change the relation of the ions in the surroundings fluid, their juices accommodate to the new equilibrium. It is probable, though this has not been investigated, that this is true also for a great many other species of marine forms. In this way one is enabled to change the blood composition of marine animals, perhaps also of fresh water ones, without doing anything else than changing the salt relation when one changes the surrounding medium.

The scientific analysis of the effects of the salt components on vital functions did not begin with the study of entire animals, but of isolated organs. It is generally known that Koelliker employed to moisten his living preparations a solution of common salt of a fixed concentration instead of tap water. But also in this physiological salt solution muscles and nerves soon lost their excitability and the cardiac pulsations soon ceased.

It is also generally known that Ringer recognized the necessity of the addition of small amounts of calcium and potassium chloride to the NaCl solution. The empirically found quantities of these salts bore again the same relation to each other as in sea water.

It was Jacques Leob who introduced a guiding idea in experiments of this kind. Based on his discovery that the fibrillary twitchings of muscle which occurred in pure NaCl solutions may be prevented by small additions of CaCl, he proposed the hypothesis of the antagonistic effect of ions.

The effect of one ion, necessary in itself but injurious when present alone, will be neutralized by the presence of one or some other ions. Leob referred to this as a detoxication. In this connection the most favorable solutions are those in which the useful and the injurious effects of all the ions present are brought into equilibrium.

According to the investigations on isolated organs of vertebrates it almost seemed as if there were only one favorable solution, and this would be diluted sea water with most of its Mg omitted. Indeed, the Mg may be absent without injurious effect. Diluted sea water with full Mg content, which Quinton believed could be used instead of Ringer's solution, is slightly injurious to the higher vertebrates. For, as Meltzer and Auer first demonstrated, excess of Mg has a narcotic-like effect on those animals. But for a great many of the mar-

ine invertebrates a relatively high Mg content is found an essential condition of life. It is not by chance merely that they have a Mg content nearly as great as that of sea water, and they die if they are deprived to a certain extent of their Mg.

Even this fact alone proves that the antagonisms of ions is not governed throughout by the same conditions. In order to investigate this point further, different methods have been selected. In the first case an attempt could be made to substitute each ion occurring in the animals by ions of similar valency, or secondly, experiments on the necessary and value of the normal ions of the blood could be extended to a great number of different species of animals.

Investigations of the first kind are of purely theoretic interest, but they gave very striking results. Thus Leob, Hoeber, Lillie and others were able to demonstrate, that Ca can be replaced to a certain extent by most bivalent ions and even by small quantities of trivalent ones. But a perfect substitute for Ca is unavailable. Such investigation showed only that one part of the detoxicating effect of Ca was due to its bivalence, another part is due to the specific natures of Ca itself.

To obtain an answer to the question, whether the antagonistic effect of the normal ions depend upon general laws, it seemed best to confine our experiments to these ions. But on the other hand, experiments with these few ions in various combinations had to be extended to a great number of different animals.

The first comparative physiological investigation of the effect of different salt solutions on intact animals or their eggs or larvae, were made by Loeb, Herbst, Oswald, Mayer and others. I myself began investigations of this kind more than twenty years ago, and have continued the same (partly in cooperation with Frau Dr. Berger) in the past few years. On these I will now report.

In order to analyse the effect of mixtures of cations the effect of each when present alone combined with an anion must be known. Former authors used pure solutions of NaCl of an osmotic pressure of the normal milieu, but they were usually afraid of trying the effect of pure solutions of the other salts of sea water in equiosmotic concentration. Doing so was regarded as unphysiological and even barbarous. But indeed every physiological experiment is unphysiological, for always organisms or organs are put into unnatural conditions. I am convinced of the necessity of using pure salt colutions, and such solutions are not always very injurious. For example, we found animals which lived much longer in pure CaCl solutions than in those of NaCl and nearly as long as in balanced solutions with the composition of sea water. You will see in Table I. how differently solutions of single salts affect the duration of the life of some animals.

Table 1.

Na Cl = 100.

	K	Mg	Ca	Artificial Sea water
Rhizostoma ..	1	2	17	4,800
Phoronis	4	90	250	33,000
Idotea	2	40	13	2,000
Daphnia	2	12	45	290
Cyclops	7	47	75	2,000
Tadpole	5	4	9	240
Tinca	34	260	390	440

Artificial Sea Water = 10,000

	Na	K	Mg	Ca
Rhizostoma ..	210	2	4	30
Phoronis	30	1	20	70
Idotea	500	3	200	70
Daphnia	3,400	56	410	1,500
Cyclops	500	33	230	380
Tadpole	4,100	200	160	370
Tinca	2,300	750	6,000	9,000

In the upper part of the table the duration of life in NaCl solution is valued at 100; in the lower part the duration in artificial sea water is valued at 10,000. Here it is at once obvious

that the tolerance of the experimental animals to the different single salts differs very greatly. From a knowledge of the effects of each single salt no conclusion can be drawn as to how these salts will act if combined in pairs, and still less if three or four salts are present. Even for simple physical properties no such predictions can be made. A good example of this is furnished by the melting points of mixtures of two substances, each of whose melting point is known. There is no general law that will tell us what the melting point of such a mixture will be.

The relations of the functions of organisms are generally much more complicated, so that it seems far too early to attempt to calculate the effects of salt combinations as Rubinstein did. Only experiments can decide the question. For this purpose one has to combine two salts in varying proportions. This will show whether their toxic effects neutralize or reinforce each other, and where the maximum of their mutual influence is exerted.

In the following figures I have restricted myself to the duration of life in different salt combinations. The observation of other functions, such as swimming, breathing and cardiac rhythm, etc. gives similar curves. To enable comparison the maximal duration of life is always made 100. The values on the abscissae signify the proportions of two isomolecular salt solutions. At the one end, the left for example, the duration in one solution alone is given. Its amount falls and that of the other salt rises, till at the right side the other solution in pure form is seen.

I speak first about the combinations of NaCl with each of the two bivalent cations of sea water Ca and Mg. In the combination of NaCl and CaCl (Fig. 1) a very distinct optimum is seen when there is much Na and little Ca in the case of four species of animals, namely the tagpole, the marine fish Gobius and two crustaceans, one from fresh water (Daphnia) and the other a sea form, Mysis. The prolongation of life by Ca is very different in degree and the optimal combination falls at different concentrations. The fresh water fish Tinca reacts quite differently to these four. Here an optimum is lacking and the curve mounts steadily from the pure NaCl solution to the pure CaCl one.

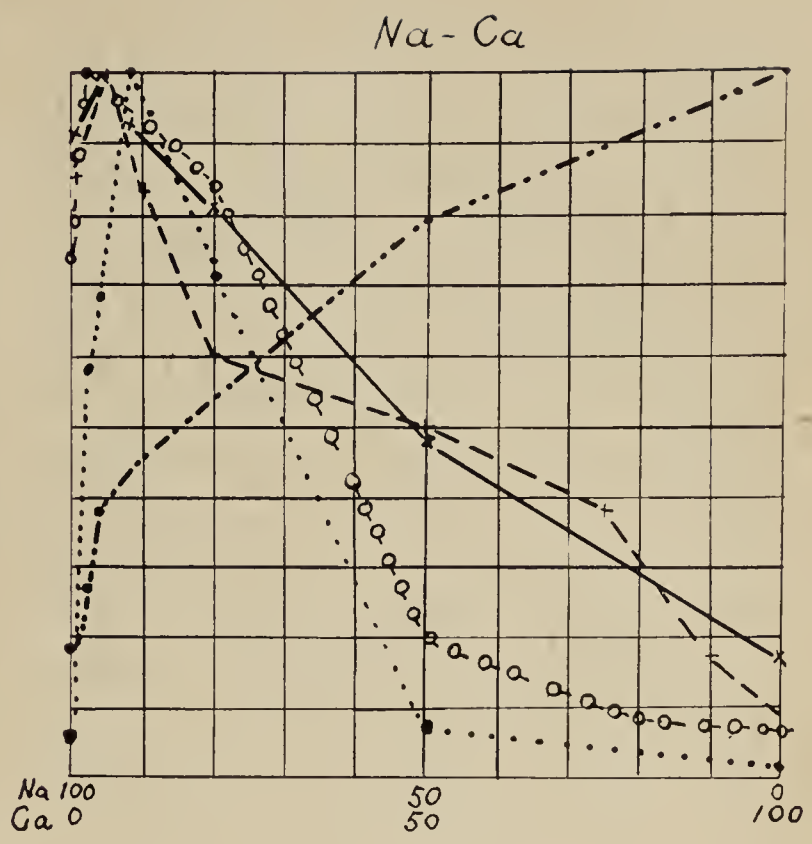

FIG. 1.

Explanation of Figure 1.

o— o— = Tadpole
.. — .. — = Tinca } fishes
— — — = Gobius
.. .. .. = Daphnia } crustaceans
——— = Mysis

The curves with combinations of NaCl and MgCl are quite similar, but the optima deviate considerably and are placed closer to the pure MgCl. This means that greater quantities of Mg than of Ca are necessary to neutralize the effect of Na. Tinca forms again an exception. Ca and Mg act as antagonists to Na in the same manner. This probably depends on their bivalency. The specific properties of the two ions are only evident if they have to act against each other, as I will show subsequently.

Let us now turn to the combinations of the other monovalent ion K with the two bivalent ones. Here also the antagonisms of Ca and Mg are similar but quite different to that with Na.

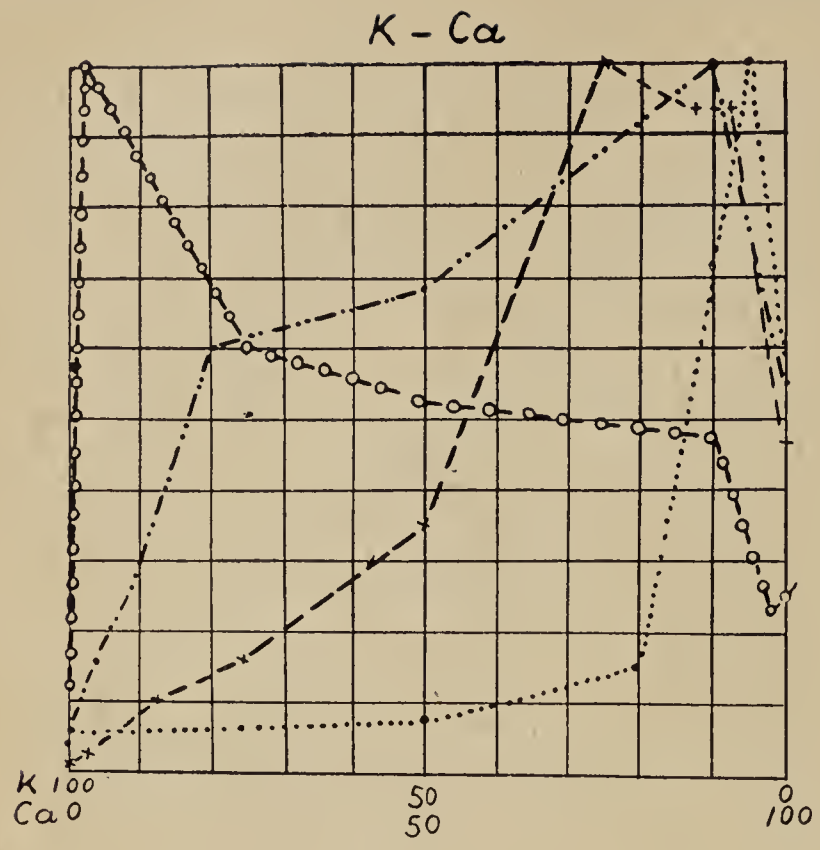

FIG. 2.

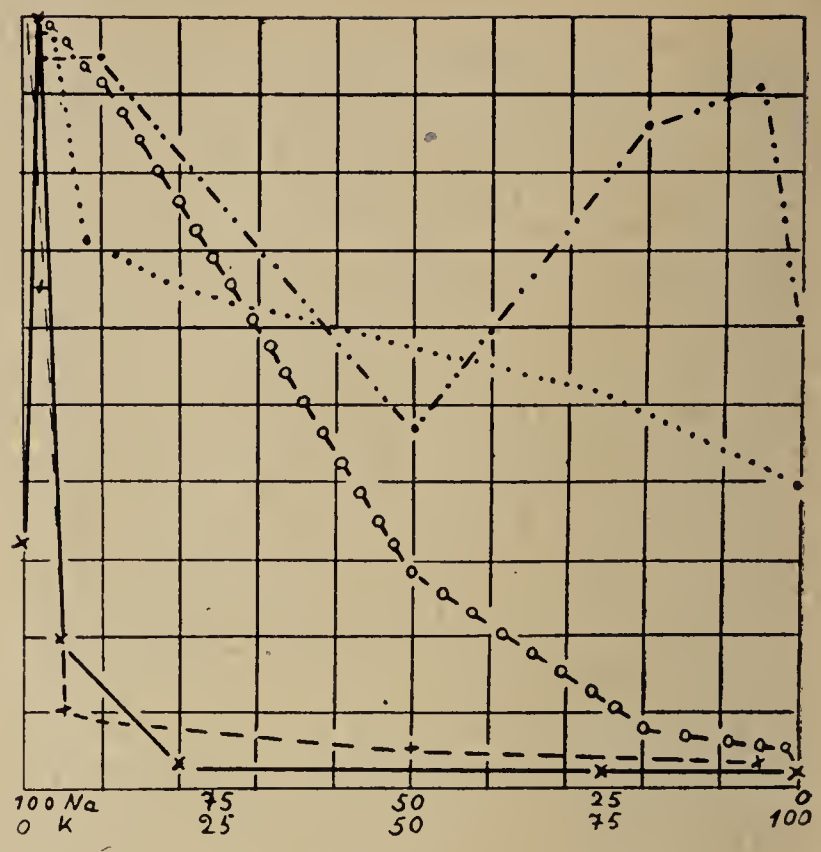

FIG. 3.

Explanation of Figure 2.

o— o— = Tadpole
.. — .. — = Tinca } fishes
— — — = Gobius }
.. .. .. = Daphnia } crustaceans
———— = Mysis }

Explanation of Figure 3.

o— o— = Tadpole
.. — .. — = Tinca } fishes
— — — = Gobius }
.. .. .. = Daphnia } crustaceans
———— = Mysis }

The optima of four species of animals are again near to one another (Fig. 2). But in this case Tinca is one of the four and the tadpole holds the exceptional position. The tadpole shows a well marked optimum with much K and little Ca. The optima of the other four, though lying in different places, are all where there is much Ca and little K. A similar result is obtained with the combinations of KCl and MgCl save that here the optimal zone of the tadpole is broader and removed more to the right.

Now let us turn to the combinations of the two monovalent and the two bivalent cations. If one makes experiments in which NaCl and KCl act in different quantitative relationships on animals, most of them (and more species were investigated than are represented on the curves) show no prolongation of life by any addition of KCl to NaCl (Fig. 3). A very small improvement is shown by the tadpole and a very considerable one by Mysis. Again Tinca takes an exceptional position as it shows a distinct minimum when Na and K were in about equal proportions. This is the only case where we got evidence of a marked addition of the toxic properties of two ions.

The differences in antagonism to the toxic effects of NaCl solutions appeared most strikingly in two species living in the North Sea, near each other and therefore under entirely similar conditions. These are the fish Gobius and the crustacean Mysis. The duration of life in Mysis is considerably prolonged by a small addition of K but not that of Gobius. On the other hand, the vital state of Gobius is obviously improved by the addition of Ca but not that of Mysis. If both species of animals are kept in the same tumblers in two series of experiments, one Na and K, the other Na and Ca, the Gobius if the relation of the two salts is correct, are dead while the Mysis continue to swim about in a lively fashion for a long time. While in the other tumblers

in the NaCa mixture the Mysis die while the Gobius are still vigorous. For Mysis K is next to Na the most important ion, depressing the toxic effect of Na, while in the case of Gobius Ca is absolutely necessary to neutralize Na.

Ca and Mg act, as shown, as antagonists to the monovalent ions. But if Ca and Mg act at the same time the differences between them are prominently shown. Their mutual antagonism is evident with varying distinctness with different species of animals, and in different proportional mixtures. Thus with Daphnia a very distinct optimum is shown with much Ca and little Mg, with the tadpoles and Mysis, with much Mg and little Ca. With Gobius a distinct optimum is lacking. In this animal the neutralizing effect of Mg against Na is nearly as great as that of Ca.

All these experiments in which only two salts of the sea water are employed represent unnatural conditions, especially for marine animals. With fresh water animals, waters may occasionally occur in which two cations are prevalent but even in this case the optimal relationship will be rarely realized. In the same water animals will live and prosper side by side, for whom the optimal conditions are not the same, as for instance tadpoles and Daphnia. If conditions corresponding to the above occur but seldom, such experiments illustrate nevertheless best of all how different the antagonism of ions may be in different species of animals.

On combining all four sea water salts, conditions become considerably complicated. As yet we have only experimented with tadpoles. The plan of these experiments was as follows: We used two pairs, each consisting of one monovalent and one bivalent ion, as Cl salts mixed in equal parts. Mixtures of two pairs of salts were presented in different combinations. Thus if one pair were formed of K and Mg the other was composed of Na and Ca. In the other case the pairs consisted of K and Ca and of Na and Mg. The mixtures so formed have in no combination the relations of salts found in sea water. But they give strikingly interesting results demonstrated in the curves of Fig. 4. The thin lines show curves already known to us, that is, the effect of K—Ca and Na—Ca solutions on tadpoles. The points on the upper margin indicate the situation of the optima of the other binary mixtures. If now the two pairs of cations are varied in the same manner as previously the salts of the single cations, curves are found with a very broad maximum. The curve of the pairs K—Mg and Na—Ca is seen to be nearly symmetrical to the curve of the pairs K—Ca and Na—Mg. So that the combined action of all four cations produce a very far-reaching compensation of their effects in a wide range of mixtures.

As already mentioned, the mixture-combination which would represent sea water, does not occur in these experi-

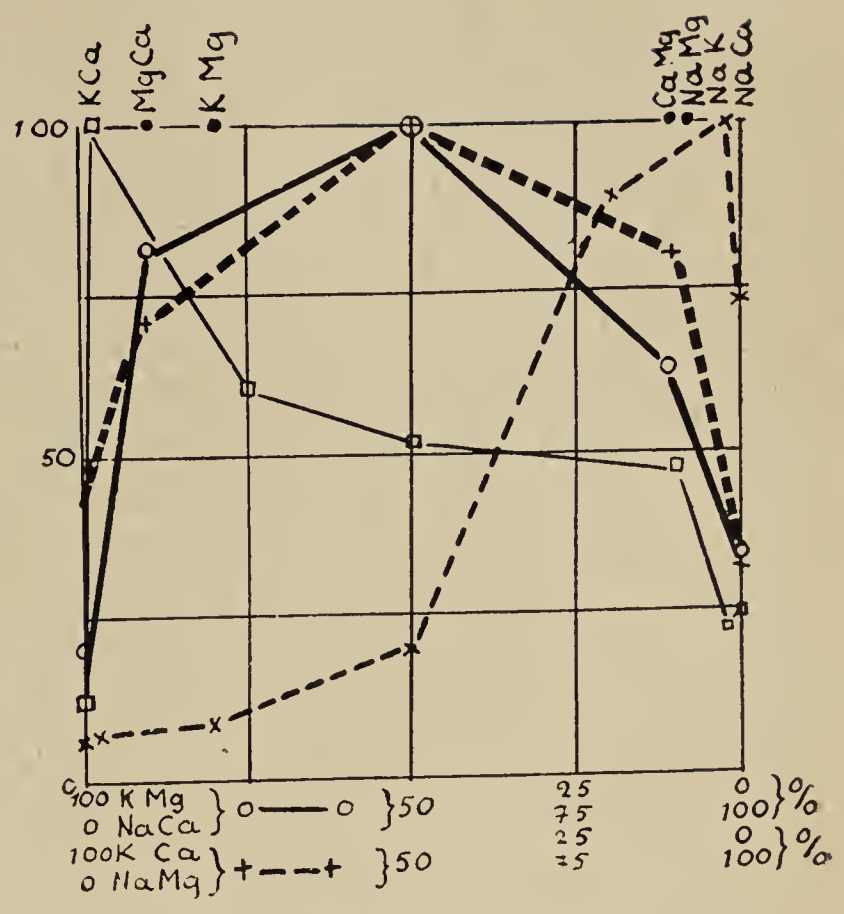

FIG. 4.

Explanation of Figure 4.

0— 0— = Tadpole
.. — .. — = Tinca } fishes
— — — = Gobius
.. .. .. = Daphnia } crustaceans
——— = Mysis

ments. In sea water the ions K, Ca and Mg are present in much smaller amounts than Na. It is to be expected that all animals are adjusted most exactly to the quantity of these four ions which occur in sea water. This opinion is based on the assumption that all animals are supposed to have arisen in sea water, and therefore they strive to maintain a relation of the ions of the blood to each other similar to that of sea water. In how far the differences in the antagonism of the ions to each other become manifest in these special mixtures, is best shown in experiments in which sea water is reconstructed from its individual components.

Experiments of this kind were first undertaken by Loeb, Herbst and Ostwald. An NaCl solution serves as the base to which the other salts are successively added in the proportion in which they occur in sea water. In this way we obtained eight different solutions, the first with only one salt NaCl, three with two salts, three with three salts and one with all four salts. In Table 2 the duration of life in the different solutions is expressed in percentages of the duration in NaCl. Here the differences in the importance of the individual ions on the different species of animals appear distinctly.

TABLE 2.

	Na K	Na Ca	Na Mg	Na K Ca	Na K Mg	Na Ca Mg	Na K Ca Mg
Daphnia	12	16	21	18	19	20	30
Gamarus	15	14	8	32	25	15	250
Phoronis	9	10	15	86	8	160	3,000
Tadpole	24	25	14	42	39	52	52
Tinca ..	27	26	17	288	108	—	300
	K	Ca	Mg				
Tinca ..	13	360	65				

A few general conclusions may be drawn in regard to the specific effect of the individual cations. In every case Mg particularly, if given in excess has a paralying action. In the higher animals which contain but little Mg in their blood, even small additions of Mg to the blood produce a condition resembling narcosis. On the other hand animals which contain large amounts of Mg in their blood, and this group contains most marine invertebrates, are markedly injured by reduction of their content of Mg, because the stimulating effect of the other cations is not any longer suppressed by the Mg. Thus it happens that some species of animals, for example the Medusa Polyorchis, are paralyzed after a short period of excitement in sea water free from Mg. In most other marine animals the evidences of excitement last a long time and only later a spastic paralysis occurs. The effect of the other cation, if present in too great or too small a concentration, often differs in different species. Thus Ca and K in excess can produce systolic or diastolic arrest of the heart. Ca also produces different effects on the central nervous system. Lack of Ca increases the excitability in vertebrates to tetanus, while in invertebrates it produces diminished excitability. On the other hand, in invertebrates an increase in the Ca in the blood causes increased excitability, which in crustaceans leads to real convulsions.

The opinion which has been frequently advanced, that the antagonism of the ions is governed by general laws does not prove to be correct in full extent, as soon as the experiments are extended to the whole animal kingdom. The fact rather appears to be, as Loeb already has proved in a few cases, that various species of animals show differing adaptations and that in some cases the one ion, and in other cases another predominates in its antagonistic effect on the other ions.

The Present Conception of Essential Hypertension*

By ARTHUR STANLEY GRANGER, M.D.
Los Angeles.

It is rather remarkable that the clinical study of blood pressure, a subject on which so much stress has been placed in recent years, should have had its inception only forty-eight years ago in the work of von Basch with the first sphygomomanometer, though Vierordt's attempts to measure the compressibility of the pulse were made years before and Richard Bright scented the condition in his monograph on the disease bearing his name. In 1886 Flint mentioned the association between chronic interstitial nephritis, the resistance to the flow of blood through the small vessels, left ventricular hypertrophy, and increased arterial tension. The first contributions to the literature in this country dealing with observations on human blood pressure were made by Richard Cabot in 1903 and 1904. Instruments free from error for measuring the pressure were not in use until 1901, and the auscultatory method was described by Korotkow in 1905.

Since the common use of the sphygmomanometer, physicians have been observing a certain group of patients in increasing numbers who show hypertension unaccompanied by nephritis, hyperthroidism, aortic insufficiency or any other condition usually associated with a rise in the blood pressure. To this type the name primary or essential hypertension has been given in this country, and also primary hypertensive cardiovascular disease by Janeway, who recognized the nonassociation of kidney disease with this type of hypertension. It corresponds to the latent angiosclerosis of von Basch, the hyperpiesis of Allbutt, the presclerosis of Huchard, and the benign essential hypertension of Volhard and Fahr. Essential hypertension is a progressive disease, probably beginning in the second and third decades of life and ending usually from the third decade on, by cardiac failure, cerebral accidents or renal insufficiency. Fahr estimates that approxinately 140,000 people die annually in the United States from hyperpiesia, and that about half these deaths are due to cardiac failure consequent to the hypertension.

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Probable Etiology.

There is no known etiology of this condition, but certain factors have been determined by clinical observation and experimental work which undoubtedly have a marked influence on the incidence of this type of hypertension. The more important of these factors will be briefly discused:

1. Sclerosis of the arterioles of the medulla. Cushing, in 1901, drew the conclusion from experimental work that an anemia of the vasomotor center in the medulla caused a systemic hypertension, and formulated the law that "an increase of the intracranial tension occasions a rise in the blood pressure, which tends to find a level slightly above that of the pressure exerted against the medulla." Anrep and Starling found that vascular lesions in the medulla which impaired the blood supply can produce a compensatory rise in the systemic pressure, which rather tends to support the theory that anemia of the brain due to sclerosis of the vesseds supplying the vasomotor center may be a factor in the production of essential hypertension. Using the work of Cushing and Starling as a basis, Bordley and Baker investigated twenty-four cases of generalized arteriosclerosis, fourteen of which showed hypertension and ten of which presented normal blood pressure.

An arteriolosclerosis in the medulla was found in all fourteen of the hypertensive cases, while in the ten of which there was normal or lowered pressure the medulla arterioles were normal. However, this investigation does not explain the primary cause of the arteriolosclerosis, nor is it improbable from the knowledge available that a hypertension may have preceeded it. Cutler studied the vessels of the pons and medulla in the brains of eighteen individuals in whom hypertrophy of the left ventricle of the heart, without valvular disease, was found at autopsy. Fourteen of these had systolic pressures of 170 or over, and in all except one the diastolic pressure was over 95. In ten of the eighteen, no thickening of the vessels was shown on section; in four the evidence of sclerosis was slight, and four showed definite sclerosis. He was therefore able to demonstrate the absence of any relationship between sclerosis of the vessels of the medulla and hypertension.

2. Vascular neurosis and hyperritability of the nervous system. Quite a large percentage of cases presenting an essential hypertension occur in persons with vasomotor instability, the so-called nervous temperament. O'Hare states that among 300 patients with hypertension studied by him, with an average age of 51.5, 42 per cent gave a history of nervous temperament, with vasomotor weakness, epistaxis, migraine, and cold, sweaty, cyanotic hands, while the control series showed 23.6 per cent with such symptoms. Von Monakow believes that a true permanent hypertension may develop on a basis of unusual nervous instability. Alvarez spoke of cyanotic hands being a valuable sign of presumptive hypertension in his work among drafted soldiers. Emotional stress certainly is a factor in temporarily increasing blood pressure, and a state of continual emotional stress, such as many of these patients present, may influence the permanence of the hypertension. Joffe's observations on the primary vascular changes in the kidney, in essential hypertension rather speak for the theory of vascular (arterial) spasm as a causative factor.

3. Heredity and vascular neurosis. Heredity perhaps should be combined with vascular neurosis as cofactors in one theory of the causation of essential hypertension. That is, "certain individuals present certain susceptibilities in their vascular responses, which are transmitted by inheritance. These individuals gradually pass into a state of vasomotor instability, as the years go on. This may be a combination of endogenous and exogenous or environmental influences, such as are the factors concerned in spastic constipation, nervous indigestion and duodenal ulcer." O'Hare, in his report of 300 cases of hypertension, found a family history of vascular disease in 68 per cent, while in the controls such a history was present in only 36 per cent. Ohler stresses heredity and environment as prominent factors in essential hypertension, and finds that such inheritance is displayed early in life by flushing of the skin, cold, moist, cyanotic extremities, fainting and dizzy spells,epistaxis and increased menstrual flow. Barach believes that persons develop hypertension because of an underlying heredity constitutional fault. In one group of his patients, 85 per cent gave such positive history. In another group of 231, 50 per cent gave a positive history. Weitz reports eighty-two cases of hypertension in which the family history was particularly investigated. Sixty-three of these patients, or 76.8 per cent, stated that in fifty-four cases one patient, and in nine cases both parents, died of heart disease, apoplexy or dropsy. In a control series of 267 patients who did not complain of symptoms suggestive of hypertension, only 30.3 per cent gave such a family history.

There are many reports in the literature of numerous members of the same family having hypertensive disease. Rosenbloom reports ten or twelve members of one family having had high

blood pressure. Cadbury, in his study of the blood pressure of Cantonese students, states that he has rarely seen hypertension, either with or without nephritis, in an extensive practice among the Chinese. One explanation of this is the simplicity of their life, and the lack of nervous strain. The condition is therefore not handed down to their children which speaks for the influence of the constitutional or hereditary factor. Janeway, however, stated that less than half his patients gave a family history of vascular disease, and concluded that heredity is only an accessory influence in the production of hypertension.

4. Endocrine disturbances. In hyperthyroidism there is often noted a moderate hypertension, but the diastolic pressure is seldom increased. Some authorities have considered the rise in the systolic pressure to be on the basis of a vasomotor instability. However, there is no evidence of sufficient merit to show that hyperthyroidism is in any way a factor concerned in the production of essential hypertension. Likewise, the ovarian secretion has been considered by some as a factor, chiefly because of the association of hypertension with the menopause and the results of feeding ovarian extract. Both Kisch and Schlesinger, after careful studies of the blood pressure in women during the climacteric, came to the conclusion that the menopause often causes marked instability of the pressure but rarely, if ever, a permanent increase. Munk feels that in some instances the hypertension may become permanent. But when one considers that about 15 per cent of women from 42 to 58 years of age have hypertension, it will be readily seen how easy it is to confuse a true essential hypertension with the transitory rise so often noted during the menopause. Increased secretion of suprarenal glands has been spoken of as a possible factor, but a permanent increase in the blood pressure to the heights of a true hypertension does not result from repeated injections of the gland extract, and pressures, several of which have been reported in the literature, have been too few to be accepted as any proof of this theory.

5. Vascular changes in the kidney. Because of the frequency with which arteriolosclerosis of the kidney accompanies essential hypertension (it is found in practically every case), the association has made a fertile field for investigators seeking light on the question as to which may be primary. There are two main speculations arising from this association: that arteriolosclerosis of the kidney causes hypertension and, inversely, that hypertension is the cause of the arteriosclerosis. The mechanism of the first of these is supposedly obstruction in the renal circulation, giving rise reflexly to general systemic vasocontriction and consequent hypertension The other view, that hypertension causes the arteriolosclerosis, seems more plausible on the grounds of evidence pointing to the fact that increased intravascular pressure favors arterial degeneration. If this view is accepted, a high susceptibility of the kidney arterioles to the hypertension must be assumed, as the arterioles to the other organs are not, early at least, so affected. However, Jaffe's investigations tend to show that the first changes in the renal arteriolar walls are undoubtedly heightened by the fact that their lumens are exposed both to rise of blood pressure and to accumulated irritating material; the latter would not apply so much to arterioles elsewhere. Renal disease other than arteriolosclerosis has no association whatever with essential hypertension, except for the changes that may secondarily occur late in the disease leading to renal insufficiency.

6. Obesity and infection. Other factors perhaps related in a way to essential hypertension are obesity and infection. Considerable has been written concerning the incidence of obesity and hypertension. Terry reported 56 per cent of sixty-three obese women as having high blood pressure. However, hypertension is frequently found in in-

dividuals who are much below normal weight, and not all obese persons, by any means have it.

When the rôle of foci of infection, as a cause of many disease conditions, was first emphasized, enthusiasm over the results of their removal in certain cases led many to suspect that such foci bore some causative relation to essential hypertension, and this idea is still prevalent in some communities. However, infection usually lowers blood pressure and there have been no bacterial toxins discovered which, when injected, will cause a rise in the pressure. On the other hand, I have observed a few cases of persistent hypertension in which, after extraction of abscessed teeth, the systolic pressure has fallen from 15 to 20 mm. of mercury and remained so for periods as long as one year without other known cause. Billings has reported such a case. It is possible that foci of infection may influence other causative factors in hypertension and thus, secondarily, play a part. Repeated infections are almost certainly are a factor in arterial disease. Ophülus has emphasized the close relationship between arteriosclerosis and infection.

I rather favor the factors of heredity and hyperirritability of the vasomotor nervous system as being of the greatest importance in the pathogenesis of essential hypertension. An inherited constitutional fault plus vasomotor instability, with vasoconstriction, would be entirely in accord with the observations of Bordley and Baker on sclerosis of the arterioles of the medulla and with the fact that arteriolosclerosis of the renal vessels is an early change in hypertension. In my series of cases, these factors have been of paramount importance.

Pathologic Changes in Hypertension.

The most constant of the pathologic changes in essential hypertension occur in the sclerosis of the renal arteries and their branches, especially in the afferent glomerulo-arterioles. Bell and Clawson state that sclerosis of these afferent arterioles is rarely if ever seen except in association with hypertension. Fishburg found renal arteriolosclerosis in 100 per cent of his seventy-two cases. According to Jaffe, the earliest anatomic change is a dilatation of the afferent glomerular arterioles. Later the capillary walls of the tufts become thickened and undergo hyaline degeneration, followed by the same degeneration in the afferent vessels. Loehlein holds the same view. Bell and Clawson find the first change to consist in a thin layer of hyaline material under the epithelium, increasing in uneven areas, with the portion adjacent to the glomerulus being somewhat later involved than the portion near the origin of the larger vessels. These authors feel that disease of the larger renal vessels precedes that in the arterioles. The hyaline degeneration continues until the vessel walls appear homogeneous, with a loss of all histologic structure and a narrowing of the lumens.

Other organs beside the kidney show arteriolosclerosis, according to Fishberg, in the following order of frequency: the spleen, pancreas, liver, suprarenals, brain, gastro-intestinal tract and heart. Sclerosis of the larger vessels or arteriosclerosis, especially of the aorta and peripheral vessels, bears no relation to hypertension. However, some degree of atherosclerosis of the arteries of the brain and of the coronaries and hyperplastic elastic intimal thickening of the renal vessels are present frequently in essential hypertension. The aorta is practically never involved. Next to the arterioles, the most frequent pathologic change is found in hypertrophy of the heart, the left ventricle being the chamber particularly involved. The muscle may show round-cell infiltration and occasionally scars are found, particularly in those cases in which coronary sclerosis is present. In the latter instance, considerable thickening of the vessel walls is shown on section, and thrombosis with occlusion of a coronary branch

is not infrequently seen. The heart weighs more than 400 Gm. The kidneys rarely show macroscopic changes, except in the small group of hypertensive patients dying from renal insufficiency or uremia. The changes are practically limited to the arterioles described. Cerebral hemorrhage or thrombosis is not an uncommon accident in hypertension, and is the cause of death in 45 per cent. of cases of hyperpiesis, according to Romberg. In such cases, the usual accompanying pathologic change is found in the brain. Cases showing myocardial insufficiency are accompanied by passive congestion of the viscera. Bell and Clawson's analysis of 420 cases of hypertension of the essential type showed the cause of death to be as follows: myocardial insufficiency, including coronary sclerosis, 60.4 per cent.; apoplexy, 19.3 per cent.; renal insufficiency, 8.5 per cent.; miscellaneous (from intercurrent disease), 11.7 per cent.

Symptoms.

From one standpoint, essential hypertension might be considered merely as a symptom of some disease condition of unknown etiology. I rather prefer to consider it more or less as a clinical entity, feeling that it is entitled to such consideration in the same light as several other diseases falling in the same category. The one cardinal symptom, then, is a permanent systolic blood pressure of 145 mm. of mercury or over, for which no cause can be determined. Practically always, although not necessarily in the early cases, there is a left ventricular cardiac hypertrophy. These two symptoms, with the reservation mentioned, make the diagnosis certain. Some patients give no subjective symptoms whatever until the hypertension has advanced to the extent that cardiac failure intervenes. In others, complaints of headache, dizziness, nervous irritability, loss of memory, shortness of breath and palpitation are common early symptoms. Frequent premonitory signs are the manifestation of vasomotor hyperirritability, flushing of the skin, cold cyanotic extremeties, sweating and excitability. Occasionally there may be found small amounts of albumin in the urine, usually of cardiac origin. The diastolic pressure varies, but is nearly always relatively high.

Little is known about the age at which essential hypertension develops. Fifteen per cent. of my patients have been under 40 years, and it may be assumed that the condition was present long before its discovery. The course is variable and the disease may go on for years without serious symptoms. Billings observed a patient who had a systolic pressure of from 200 to 260 mm. of mercury for 40 years without a serious break. Sooner or later, however, signs of cardiac failure, cerebral vascular changes or renal involvement, develop. These organs are involved as to frequency in the order named. When cardiac failure occurs, the signs are the usual ones accompanying such a condition from any cause. Headache and dizziness are often warnings of approaching cerebral hemorrhage or thrombosis. Uremic manifestations are the usual signs of renal involvement.

Differential Diagnosis.

Essential hypertension must be differentiated from the high blood pressure secondary to glomerulonephritis, certain nephroses, arteriovenous aneurysm, toxemia of pregnancy, the hypertension of the menopause and other forms of transitory rise in the pressure. In glomerulonephritis there is seldom the amount of cardiac hypertrophy seen in essential hypertension; there is secondary anaemia, and in advanced cases there may be edema and dyspnea, but no passive congestion of the liver. The nephroses offer no difficulay in differentiation. In urinary obstruction there are usually definite signs of the obstruction or evidence of some spinal cord lesion causing it. In hyperthyroidism there is an increased pulse pressure due to the wide diver-

gence between the high systolic and low diastolic pressures, together with the usual symptoms of the thyroid hypersecretion Aortic insufficiency usually shows the loud diastolic murmur, with other signs in the pulse characteristic of this condition. In the toxemia of pregnacy there is no cardiac hypertrophy, and the blood pressure, in the simple form, returns rather quickly to normal after the uterus has been emptied. The transitory forms are distinguished by their very variable pressure readings.

Prognosis.

The prognosis is hard to gage. Some of the early cases pursue a rather rapid course and seem to be subject to cerebral or cardiac accidents. On the other hand, in many of the cases the conditions continue for years, even beyond the normal expectancy of life, and finally death occurs from some intercurrent disease. The ability of the myocardium and the cerebral vessels to withstand the strain of the continued pressure is probably the essential factor in the prognosis. A high diastolic pressure has, in my experience, been of serious import. Neither the vessel nor the heart seem able to withstand a diastolic pressure of 120 or more for any great length of time. A change in the rate of the heart's contraction, from a comparatively slow one to a persistently rapid one of 100 or more, is rather an indication of approaching myocardial failure. Definite changes in the retinal vessels often indicate renal complications or the chance of some cerebral vascular accident. Death usually is from cardiac failure. According to Christian's statistics, 32 per cent. die of cardiac failure, 25 per cent. of cerebral lesions and 4.5 per cent. of uremia. Romberg states that 45 per cent. die of cardiac failure, 45 per cent. of apoplexy and 10 per cent. of uremia. In my series, 52 per cent. of the deaths have been from cardiac failure; 31.5 per cent. from cerebral accidents (hemorrhage and thrombosis); 5.5 per cent. from uremia, and 11 per cent. from intercurrent disease.

Treatment.

Essential hypertension is a progressive disease. There is no known cure, and efforts in treatment must often be directed toward relieving certain conditions of environment and habit that may appear to aggravate it. In no other disease is it more essential for the physician to know and treat the patient. One of the hardest problems in therapeutics is to change a nervous temperament or other inherited characteristics of an individual: to make a patient with a worrying disposition cease to worry, or to replace an excitable nature by an even, calm one. A certain amount of prophylactic treatment can be carried out to advantage. Young people who have inherited a hypersensitized nervous system, and who may have a history of hypertension in one or more members of their family, should be restricted from too strenuous exercise and discouraged from entering careers in which a high tension life is a necessity. Especially is this so in those young people who show vasomotor instability, as stressed by O'Hare.

Treatment of the vasoconstriction is indicated before the secondary changes in the heart and kidneys occur. When hypertension has developed, much can be done toward prolonging life and preventing complications by proper regulation of the life and habits of the individual. Foster believes this can be best accomplished in many of the early cases, especially by sanatorium care, as the patients may be better educated, both as to the necessity of taking care of themselves and as to the manner in which this care is to be directed.

Frequent talks between the physician and the patient often brings out factors in the patient's mode of living, business habits, habits of eating, and home and social life which may be corrected advantageously. The patient should be taught to avoid, as much as

possible, business worries, or little details that some other member of the firm or an employee may very well take off his shoulders. Annoyances and aggravations in his home life should be disposed of; his social obligations should be curtailed. An hour's rest and absolute relaxation after the midday meal are advisable. The blood pressure has been observed repeatedly to fall after such a rest. He should be encouraged to sleep at least eight hours each night. A week-end every month, spent at home, practically in bed, is a good habit to follow. Frequently vacations away from home and business relieve largely, for the time being, a great amount of nerve tension and the responsibility and worry every family man of necessity has. This regimen should be advised gradually, so as not to alarm the patient unnecessarily and make him feel that his whole future is to be that of an invalid. Moderate exercise is of benefit, especially such as will be a pleasure rather than an irksome task. Golf, walking and supervised setting-up exercises are all good, though the amount should vary according to the reaction obtained and to the ability of the individual to stand such exercise.

The diet is of little importance in essential hypertension, except when indicated by overweight or some complication, as cardiac failure or renal insufficiency. It is difficult to understand the advantage in protein or salt restriction. Mosenthal and Strouse and Kelman have shown how harmless are the effects of high protein feeding. Anderson's experiments in feeding a high protein to rabbits, both normal and partially nephrectomized, indicated no increase in the blood pressure. Protein restriction may decrease the nourishment of the individual to an unwonted extent. Salt restriction, of course, is indicated when cardiac failure supervenes. Fluids need not be restricted. Orr and Innes have shown that liquids, up to 6 liters a day, do not influence the pressure. Purgatives are of no value, except when complications of the heart or kidney occur. The idea of regularly taking saline cathartics is distinctly annoying to most patients and is just as distinctly unnecessary. Alvarez and his co-workers have demonstrated that constipation and so-celled intestinal autointoxication bear no relation to hypertension. It is well to restrict the diet in the obese individual, but the restriction should be mainly in the carbohydrates and fats. Faber's statistics indicate that a fall of from 15 to 20 mm. in the systolic pressure occurs with a loss of from 8 to 16 pounds (3.6 to 7.3 Kg.) during the treatment of obesity. Terry states that, on a high protein, low calorie diet, obese persons with hypertension both lose weight and show a lowering of the pressure.

Drugs have but little place in the treatment. Bromides may help in lowering the nerve response to various stimuli in the hypersensitive nervous individual. Iodides, perhaps, through their effect on metabolism, may be of use in some cases. For tiding the patient over undue rises in the pressure, I have found sodium nitrite, in 1 grain (0.065 Gm.) doses, three times a day, very valuable. A fall in the systolic pressure of from 10 to 25 mm. has been repeatedly observed. Continuation of this drug, over a period of weeks, has, in certain cases, never shown harmful results. When coronary disease is superimposed, the various preparations of theobromine and theophylline are of value. When cardiac failure occurs, digitalis is often of distinct benefit. I believe it has never been shown to have any effect toward raising the pressure in these hypertensive cases. For the cardiac edema, I have obtained the best results from the use of merbaphen intravenously. The promises of any permanent effects from the use of hepatic extract have not been fulfilled.

It is also a question as to how much should be told the patient of his condition. I feel that this should depend entirely on the type of the individual with whom one has to deal. A certain class of patients evidently should not

be informed of their weekly or monthly blood pressure readings. In my experience, however, this class is small. Better co-operation between physician and patient is obtained in the vast majority of cases by a frank discussion as to just what one is attempting to accomplish by the treatment prescribed, and a much better understanding of the causes of transitory rises in the pressure is given if one has the patient's entire confidence.

Summary and Conclusions.

1. Essential hypertension is a condition characterized by a persistent systolic blood pressure of 145 mm. of mercury, or over, and a left ventricular cardiac hypertrophy, without demonstrable cause, though the hypertension may exist in the early stages without the cardiac enlargement.

2. There is no definite cause for this condition. The factors most concerned are heredity and vasomotor hyperirritability. Vascular lesions of the medulla, affecting the vasomotor center, probably may produce a rise in the systemic pressure, but there is no proof that a hypertension does not precede such lesions.

3. Sclerotic changes in the afferent arterioles of the renal glomeruli are almost pathognomonic and are the most common pathologic finding.

4. The height of the diastolic pressure is probably of greatest moment in determining the prognosis. The cause of death, in a series of patients with essential hypertension, was cardiac failure in 52 per cent. cerebral vascular accidents in 31.5 per cent. uremia in 5.5 per cent. and intercurrent disease in 11 per cent.

5. Treatment should be directed mainly toward a regulation of the life and habits of the individual, so as to promote rest, freedom from worry and aggravation, and moderate pleasurable exercise. Dietary restrictions are of use only in the obese, or when cardiac or renal incompetence occurs. Drugs have a very small field in this condition. A frank discussion of the ailment by the physician and the patient is advisable in most instances.

Some Observations on Rheumatic Fever in Children.

By GEO. R. PIRIE, M.D., M.R.C.P.

In considering the effect of specific treatment on Rheumatic Carditis, it is first necessary to have a clear idea of the nature of the condition treated.

It is admitted that many acute infections and specific fevers create pathological changes in the various structures of the heart; thus it is not always possible in a given case to say whether a suspected heart lesion is an evidence of Rheumatic Fever or not.

However, the proportion of Carditis in children that is rheumatic at least in its inception, is so large that we think of Carditis in children as a rheumatic infection.

Acute Rheumatic Fever is much more sharply defined as an entity in the adult than in the child. Thus when one finds evidence of Cardiac mischief associated with poly-articular trouble, we presume both to be rheumatic.

In the child we may find vague manifestations of an infection which sooner or later may become associated with a cardiac lesion. Moreover, we find such constancy in this association that we have come to regard them as Rheumatic in themselves. The typical attack of Rheumatic Fever as seen in the adult is most unusual, and the common situation in the child is that of a rheumatic state if we may call it so—a chronically infested state, in which any of these various manifestations may indicate the existence or beginning

of that state, but one in which, whatever the beginning, a damaged heart may be the end.

A few of these minor manifestations are, for example, the vague though sometimes severe pains in the calves, hamstrings, shins, and in the popliteal space. No apparent lesion can be found to explain them;—the persistent and recurrent headache (chiefly a morning headache) independent of eyestrain, adenoids or intestinal disturbances. Erythema multiforme is another minor evidence of this state.

We do not refer to these conditions usually as acute Rheumatic Fever. Potentially they are, in that experience has shown again and again an obviously damaged heart in a child where the only previous symptoms were such as these.

Again with chorea, we have a child an undoubted candidate for Rheumatic Carditis. So much has been written and so many statistics given to prove the infectious nature of chorea, that we will not labor the point. One constantly meets in practice the sequence of events as illustrated by a boy lately discharged from the Hospital for Sick Children. This had been his third admission to the hospital with chorea. The first two attacks were uncomplicated. The third time there was undoubted carditis on admission and he was discharged with a damaged mitral valve.

The late Dr. Batten followed up some 80 cases of uncomplicated chorea after discharge from the hospital, and found a very large proportion of them to have developed some form of carditis at a later period.

Then there are children about whom one is consulted because they, in the mother's opinion, simply are not doing well. They are languid,—have lost interest in their pursuits, both in and out of school. They are somewhat anaemic and tire easily on exertion.

Physical examination of any of these children may reveal nothing gross to account for their symptoms. On the other hand sooner or later one finds so often slight cardiac changes. The signs are found sufficiently often to make one ever on the alert to suspect possible mischief in the hearts of children presenting what may seem trivial symptoms.

The signs one finds in the hearts of these cases are nearly always, in the beginning in any event, referable to a damaged myocardium. The visible impulse is more diffuse and percussion will show a slight increase in the transverse diameter of the heart dullness. It is here that the refinement of delicate percussion is well repaid. Very light percussion is necessary as slight decreases in audibility might be overlooked if the too frequent sledge hammer technique of percussion is employed. Auscultation may reveal a soft blowing systolic murmur or internal to the nipple which is not transmitted to the oxilla.

These very slight signs must be looked for if the heart is to be spared more extensive trouble.

Some infection has caused inflammatory changes in the myocardium at any rate. The trouble may end here if we can remove the original focus of that infection and the myocardium recover. Recover it may as we know that inflammatory changes in the child's myocardium are never followed by those fibrous degentrative changes so often noted in the adult heart.

Worse than all this, there may be acute carditis with severe inflammation of all the structures of the heart ab initio.

Occasionally but not nearly so frequently as in the adult, do we find polyarticular trouble. Rarely even when present, are the joints swollen, red and painful as in the adult. This trouble may exist alone or accompany any of the symptoms previously mentioned. The joint swellings and the discomfort therefrom may be so little that it may only be discovered on routine examination of the child.

The association of sore throat preceding or accompanying any of the above conditions is too frequent to be accidental. So that now we have come

to regard frequent sore throats or attacks of Tonsilitis in children as the probable beginning of the more obvious signs of Rheumatic Fever with possible invasion of the heart.

In any of these conditions, careful examination should be made for subcutaneous fibrous nodules over bony prominences and along tendons, such as the Palmaris Longus. Their presence is pathognomic of heart trouble. They would suggest that signs of cardiac mischief, doubtful in themselves, are an indication of organic change. In the absence of such signs, they may be anticipated within a very short time.

In the consideration of the possible relation of focal infections to carditis surely it is more important to consider its relationship to some of these vague clinial conditions in order to prevent if possible more serious heart affections by the removal of that focus.

Whenever one finds any of the above symptoms complices, search should be made for some possible source of entry for the infection.

As mentioned before, the association of sore throats and tonsilitis is so constant, that in all cases the tonsils should be suspected. I do not think that one should hesitate to have then enucleated in any case that has presented any of the symptoms mentioned, whether there is definite evidence of trouble in the tonsils at that time or not. If they are obviously infected and if the glands which drain them remain enlarged, no one would consider this treatment unnecessarily radical. But I should like to urge that even without these evidences of local trouble, they should be enucleated, because experience has taught that these or similar symptoms are sure to recur and probably with definite and obvious Tonsillar infection. Every time the child has a recurrence of these symptoms, increases the probability of the heart becoming affected. Therefore to minimize this possibility, remove the tonsils early.

May I quote the case of a girl H. A. aged 11, who was brought to me simply because she was rather pale and preferred lying around to playing as a normal child would. On physical examination I found nothing beyond a slight degree of secondary anaemia. The tonsils appeared healthy and there was no glandular enlargement. As she had given a history of "growing pains" a few years previously, she was given salicylates and ordered increased rest. She improved rapidly and was well for about three months. Then the same symptoms recurred. The results of physical examination were the same. The same treatment was instituted. There was a further period of apparent good health of about three months. Then for the 3rd time the lassitude and pallor appeared. This time I found a slight increase in the transverse diameter of the heart and a localized fluffiness of the 1st. sound at the apex, with a somewhat exaggerated 2nd. Pulmonic sound. She was put to bed and at an opportune time her tonsils were enucleated. Before operation there was nothing whatever to indicate local trouble in the tonsils. At operation a small localized abscess was found behind one tonsil. Since then the child has gone straight ahead and has had no recurrence of any unpleasant symptoms.

The symptoms may be even less significant than these. This last spring a Big Brother brought a boy of 13 to my clinic at the Hospital for Sick Children to be examined. His teacher had complained that he was dull, stupid, and lazy. The Big Brother happened to know this boy, and knew that formerly he was an alert active lad who excelled in his classroom. I found no more on examination than in the previous case. He gave a history of vague pains occasionally occurring in his arms and legs. His heart showed the same signs. His tonsils were enucleated and in a very short time afterwards he was restored to his teacher's favor. These instances could be multiplied ad infinitum. The point I wish to make is this. These children showed slight signs of the early involvement of the myocardium, and I am sure their hearts

were saved from further and more extensive trouble by the enucleation of the tonsils. They should have been removed the first time the children complained of the so-called "growing-pains."

It may not always be the tonsils which are at fault. It has been suggested that Dental Caries and Intestinal disturbances may initiate the trouble. The opinion has been offered that a faulty and indiscreet dietary may lower the local resistance of the bowel and thus a portal of entry be found for the invading agent there. Personally, I have never been impressed by the evidence for these hypotheses. Most commonly in any event it is tonsilitis, or naso-pharyngitis—even otitis media or sinus trouble from the naso-pharyngitis.

Even when the heart appears seriously damaged, much can be done. M. Z. a boy of 10 was admitted to the Hospital about two years ago. He had a marked degree of Aenemia, became breathless on the least exertion — in fact he could do very little at all. These symptoms had been gradually becoming more pronounced during the previous year.

Examination of his heart showed considerable dilatation and a double bellows murmur at the apex.—the systolic one being transmitted to the axilla. When the time was considered opportune, the dental caries was cleared up. Later on his tonsils were removed.

The boy was in my clinic a few weeks ago, and strangers who knew nothing of his history could find no evidence of cardiac trouble whatever. He goes to school and engages in all the usual pursuits of his age without any embarrassment.

Unfortunately this does not always happen, but it does happen with sufficient frequency to warrant one in dealing with dental caries and tonsils in every case.

Removal of these foci does not guarantee complete immunity against future attacks. But at least it does minimize the possibility of recurrences.

If the tonsils are to be removed, care must be exercised to choose the proper time. Nothing may be done until all evidence of acute infection has subsided. If there are carious teeth, these must be attended to first, otherwise the removal of the tonsils first, opens up a large absorbing area for the infection from the teeth.

The temperature may be taken as a safe guide as to when to remove the tonsils. It is my own practice to wait until the temperature has remained below 99° F. for at least two weeks. The following case illustrates the importance of this.

M. L. A girl of 7 had been having frequent attacks of Tonsilitis. On this account her physician had advised the removal of the tonsils. Several times the surgeon was about to remove them but there was a slight elevation of temperature, so the operation was postponed. Finally they were removed. In justice to the surgeon it must be said that he did not know, that on the morning of the operation, the temperature was 99.5° F. 48 hours later I saw her and she was running a temperature around 103° F—the pulse was rapid and she had an acute carditis. This child spent the next six months in bed. This is the third similar case in my own experience.

On the other hand, there is at present in the Hospital for Sick Children a girl recovering from an attack of carditis. She had a severe infection showing Endocarditis, Myocarditis and Pericarditis. We waited until the temperature remained below 99° F for two weeks. The tonsils were then enucleated without any unpleasant reaction of any kind whatever.

Moreover the tonsils must be removed completely. That is, the pharyngeal and the lingual prolongation of the Pharyrgeal Tonsil must be removed. It makes no difference what method of enucleation is employed so long as it is all removed. If the lingual prolongation is left, as it so easily may be, later on it may become the seat of an infection with disastrous results. The fol-

lowing case illustrates this point. L. S. a boy about 14. Four years ago he had his tonsils enucleated on account of repeated attacks of Tonsilitis. There was no history of Cardiac involvement at that time.

For the next three years he led a very active life at school. He was captain of his school hockey and football teams, and had won one of the inter-school sprints.

Last winter he had an acute attack of sore throat followed by acute joint and muscle pain. I saw him in January when his temperature was ranging from 103-105° F. There was poly-articular Rheumatism and an acute carditis.—the usual picture of adult acute Rheumatism Fever. On examining his throat, there was some tonsillar tissue on one side—red, swollen and showing some ulceration. The whole pharynx was also congested. It is probable that here was the focus of infection. The tonsil had been incompletely removed three years previously.

It was four months before that boy's temperature became normal and his heart compensated. When I saw him last, before transferring him back to his own physician there was a valvular lesion, which he will always have.

One never knows when a tonsil once infected may become so again. Each attack increases the danger of the involvement of the heart. If the heart is once involved, it itself may become the seat of infection and every time the child is below par from any cause, the focus in the heart is almost sure to flare up with further damage to that organ.

Although maintaining an open mind on the subject, it would seem to me that a heart once damaged is more prone to show active trouble again following some new infection than following too much strain.

I think one may safely conclude by urging that a child showing any symptoms which may indicate an infection that may be followed by carditis should have its tonsils enucleated and any other focus or portal of entry of infection cleared up. In a large majority of cases this will prevent the recurrence of infections leading to a damaged heart. If the heart has been involved as to the Myocardium only, their removal will probably prevent any extension of trouble in the heart. Even if the Endocardium has been seriously involved, their removal at least minimizes the possibility of the recurrence of infection in that heart, and gives it its best chance to achieve compensation.

Paget's Disease of the Nipple.

By RUSSELL K. MAGEE, B.A., Med. '30.

History.

Paget's disease of the nipple is named after Sir James Paget, who gave the first clinical description in the St. Bartholomew's Hospital Reports in 1874. It was, however, first mentioned by Velpeau in Leçon's Orales de Clinique Chirurgicale in 1840. No disease of equal rarity has given rise to such divergence of opinion, or gathered round itself such a mass of literature, possibly because in it men saw a disease, the closer study of which, might lead to a solution of the greatest of medical enigmas, the etiology of Cancer. Accordingly it has been used by Handley to substantiate his theory, and men have used it to support Guy and Bernard's theory, to which mention will be made below.

Anatomy and Histology.

As the investigation of Paget's disease necessitates a minute anatomical understanding of the breast and nipple we will review in brief the essential points. The mamma consists of gland tissue, and fibrous tissue connect-

ing the lobes, and fat. The subcutaneous tissue encircles it and sends septae in between the lobes. From the fascia over it fibrous processes pass forward to skin and nipple. The lobules consist of alveoli opening into the lactiferous ducts, 15-20 in all, converging to the areola beneath which they form ampullae or dilatations. The ducts are lined by a single or double row of low columnar cells. Beyond the ampulla the duct epithelium changes to stratified squamous, continuous with the cutaneous surface of the nipple. The alveolar epithelium varies from a mass of glandular polyhedral cells, in nonpregnant state, to an active state in lactation when central cells undergo fatty degeneration and the peripheral cells become larger and remain as short columnar cells with spherical basal nuclei. In cancer the hard contracting tumour drags on the fibrous septae between the lobes so that fixation and retraction of the nipple ensues.

The skin over the breast, as elsewhere, is made up of epidermis, dermis, and subcutaneous tissue. The epidermis is stratified squamous epithelium and is divisible into horny, cornified corneum, and the deeper layer, the rete Malpighii of cylindrical and polyhedral cells. From inside out the layers of the rete are columnar cells, then prickle cells with intercellular fibrils visible, which dip into the dermis between the papillae. The dermis has projections or papillae extending into the epidermis, but separated from it by a delicate elastic and fibrous basement membrane.

The lymphatics of the skin start as blunt finger-like culs de sac in the dermal papillae. These drain in narrow vessels uniting in the deeper dermis to a collecting vessel which passes vertically through the subcutanteous fat to the fascial plexus.

Clinical Picture.

There really has been little added in fifty years to the original description of Sir James Paget. It is quoted here as it is impossible to summarize; for it possesses in the highest degree those virtues of conciseness and concentration.

"I believe it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhous cancer in the mammary gland. I have seen about fifteen cases in which this has happened, and the events were in all of them so similar that one description may suffice. The patients were all women various in age from 40-60 or more years, having in common nothing remarkable but their disease. In all of them the disease began as an eruption of the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed, like the surface of very acute diffuse eczema or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple and areola, there was always copious clear, yellowish, viscid exudation.

"It has happened that in every case I have been able to watch, cancer of the mammary gland has followed within at the most, two years, and usually within one year. The eruption has resisted all the treatment, both local and general that has been used, and has continued even after the affected part of the skin has been involved in the cancerous disease.

"The formation of cancer has not in any case taken place first in the diseased part of the skin. It has always been in the substance of the mammary gland, beneath or not far from the diseased skin, and always with a clear interval of apparently healthy tissue."

The earliest sign is on the nipple, rarely on the areola or skin, in the form of a florid eruption which spreads over the entire nipple and some of the areola, but rarely beyond this. The area is slightly indurated, and sharply demarcated in outline, thus differing in

outline, histology, and in response to treatment, from ordinary chronic eczema. It differs from squamous carcinoma, which is hard, elevated, with everted margins and which lacks the smoothness and bright colour of Paget's disease, which does not invade the dermis. The nipple may become flattened and disappear and itching may be noticed. If itch, pregnacy, and eczema are excluded, and if the patient is over 40 years of age, and if the lesion has persisted over 3 weeks to 3 months—it is Paget's Disease.

Constant Pathological Picture.

The microscopic picture presented in this disease is constant and is readily recognized. It may be briefly tabulated as follows:

1. Epidermal hypertrophy to 2-3 times normal thickness ahead of the advancing margin or before ulceration.
2. The papillary bodies are deeper and thicker and encroach on the connective tissue papillae which are narrowed.
3. Sub-epidermal round celled infiltration of lymphocytes and plasma cells; corresponding to the affected area of epithelium. (Feels like a coin buried under the areola).
4. The pathognomic picture of the disease is the presence of so-called "Paget's cells," which were not mentioned, however, by Paget at at all. These cells are large, with clear vacuolated cytoplasm, a large nucleus, no prickles, showing no cornification. The protoplasm is granular and less chromophilic than the malpighian cells. The centre may be homogeneous and acidophilic while the periphery is spongy and basophilic. Nuclei are large, vesicular with 2-3 large nucleoli, and hyperchromatic.

The Nature of Paget's Cells.

The whole subject of Paget's disease hinges on the nature and origin of these pathognomic cells, and many and varied are the theories attached to them.

They have been thought to be degenerated prickle cells with nuclear changes, loss of fibrillation, vacuolation, compression, and diminished cornification, losing their characteristics due to irritating discharges of ducts and ulcerated surfaces.

A typical multipolar karyokinesis has been seen and Pautrier saw Paget's cells destroying Malpighian cells, behaving like neoplastic virile invading cells. The Paget cell is seen actively invading the prickle cell, with its connecting fibrils and nucleus still intact. With 1,000 mangnification and both in exact focus he says it cannot be an artefact and both must be on the same plane. He says the young Paget cells are "destructive and migratory" and the old ones are passive and carried up by ascending Malpighian cells. He says the so-called "mantle cells" are Malpighian cells invaded by Paget's cells, the Malpighian cells cornifying to form the mantle.

Masson states there is possibility of active migration of cancer cells from breast cancer and Paget's into the epidermis, and shows as well as typical spherical cells, some with lobulated cytoplasm like leucocytes in amoeboid movement.

The Various Theories.

The theories that have been advancer in this disease are so many and so instructive as to its pathology that a few of the more valuable may be mentioned.

The fact that Paget's description did not include the histopathology has been responsible for much of the confusion. Some authors thought the key to the solution lay in histological study of extra mammary forms. As the number of lacteal ducts showing carcinomatous degeneration is not large and may be limited to one duct, the present feeling is that the solution lies in histological study of serial sections of the entire nipple in early cases.

The various theories chiefly concern

themselves as to the origin and mode of spread of the Paget cells and their relationship to the clinical finding of carcinoma. They range from a theory that it was due to a coccidia, a dyskeratosis, lymphatic obstruction, up to the present view of it being primary intraduct carcinoma. We will enlarge on each of these theories independently under the headings of the various investigators who have been responsible for them.

Paget in 1874 suggested the chronic superficial disease induces degeneracy in the structures beneath, making them susceptible to carcinoma, but he did not enlarge on this theory.

Thin in 1881 was first to show the distinction between the skin changes and true eczema, and claimed it was secondary to duct carcinoma, due to a toxin elaborated by the cancer cells.

Darier and Wickham in 1889 first observed Paget cells, but thought them coccidia. This was disproven by Unna —who thought them precancerous degenerated prickle cells.

Jopson and Speese thought it a primary condition starting in rete malpighii and occurring elsewhere than the breast and only potentially malignant, commonly but not always followed by carcinoma.

Arnd thought it a precancerous condition, and due to infiltration of the cells with glycogen.

Kilgore thought it spread from the skin into the ducts, but concluded it could spread in either direction. His sections support Muir's theory given below.

Jacobeaus in 1905 said, "It is cancer from the outset, and arises in the gland epithelium of the duct. The changes in the skin are due to proliferation and extension into the skin of cancer cells originating from gland epithelium. The late appearance of carcinoma points to the benignancy of the primary affection due to obstruction to growth by connective tissue." It is to Jacobaeus that many aspects of the present conception are due.

Ribbert and Schambacher agreed with Jacobaeus and based their views on the association of the Paget's cells and cancer on histological section, and the changed appearance of the Paget's cells from prickle cells.

Darier renounced his first coccidial theory, but came back with that of Dyskeratosis—defined by him as "Faulty development of epidermis in the course of which a certain number of Malpighian cells become isolated and differentiated from their fellows, undergoing an abnormal premature, keratinisation." In 1914 he designated four diseases as dysknotoses—Bowen's disease, Paget's disease, Darier's disease and Molluscum Contagiosum. The evidence against this view is given by Fraser and is mentioned below. However, Darier exerted a powerful influence on the thought of the French school and dermatologists.

Bloodgood differentiated Paget's from numerous benign lesions. His studies in light of present day knowledge support Muir's theory given below. He reports cases outside the limits of Paget's original description—in one the whole breast had ulcerated, another ulceration for 3 years and no palpable lump, and another case of ulceration existant for 5 years with the nipple not yet replaced.

Cheatle says it starts in the deep layers of the epithelial cells, dipping down into the duct orifices. He says acini may occur in the nipple so that all carcinoma of the nipple need not be duct carcinoma. He states that if Paget's disease were due to duct carcinoma it would be common, not rare. He believes the carcinomatous change may result from irritation of plugs present in outlets of the ducts. Because he did not find the growth continuous down the ducts and because the cells in the ducts were not exactly like those in the skin, he concluded the growth in the duct was not growing down the duct or even a transplant from the upper duct, but was merely a result of the same irritation which caused the carcinoma higher

up, acting on the cells lower down, and reaching them by means of the duct.

Handley has a most interesting theory which we will study a little more in detail, as he applies it to the origin of carcinomata in general. He considers the dermatitis secondary to a plugging of lymphatics by underlying carcinoma cells. He believes the cancer starts in the small ducts of the breast and acini and without producing a tumour, spreads and permeates the lymphatics. This spreads to the subareolar plexus beneath the nipple. By the lymphatic oedema the superficial layers of epithelium degenerate and disintegrate, and the deeper layers proliferate—a nutritional change—not a malignant one. The permeated lymphatics undergo perilymphatic fibrosis and with the surrounding infiltration squeeze out the carcinoma cells—hence — on removal these may not be seen. He considers the serous discharge a lymphorrhoea. He states chronic eczema is associated with lymphatic oedema in elephantiasis, and that the variation in Paget's disease is due to anatomical peculiarities of the nipple; and the subsequent fibrosis of lymphatics may be responsible for the retraction of the nipple.

In 1916 he found a case with lymphatics permeated by carcinoma cells and the Paget's area corresponded exactly to the area of involvement beneath, which he considers significant.

Handley is at the present time most emphatic in his support of this theory, and applies it to the origin of all carcinomata. He desires to be remembered for two things, first that he said 25 years ago that carcinoma spread by lymphatic permeation and, secondly, that he demonstrated the importance of lymph stasis in its etiology.

He theorized that when the specialized multi cellular organism arose from its unicellular ancestor it gave up its right to unlimited cell division, and that carcinoma is an atavistic reversion to its ancestral form, caused by a breach of contract on the part of the rest of the body cells in the form of lymphatic obstruction, which reduces the supply of oxygen and inhibitory hormone of cell division to the cells. It is interesting to observe that most up to date cancer research approaches the problem from this metabolic viewpoint. The lymphatic obstruction and perilymphatic fibrosis may be due to irritants, such as tar, chemicals, radiation, etc., because frequently sarcoma rather than carcinoma follows such irritation. He considers papillary hypertrophy the intermediate step in carcinoma production and directly dependent on lymphatic obstruction. He stresses the frequency with which carcinoma follows on papillomata as duct papilloma and polyposis.

Warburg has recently shown that cancer cells derive more energy from gluscose hydrolysis and less from oxidation, and this is in accord with the theory.

He theorizes still further to suggest that tuberculosis may increase precancerous tendencies, as it essentially blocks lymphatics, and Cherry in Medical Journal of Australia, shows that the incidence with which he is able to develop malignancy in rats is enhanced by subcutaneous injections of living tubercule bacilli, and points out that while the mortality of carcinoma is increasing, and that of tuberculosis decreasing, the sum of the two is relatively constant.

The chief objection to this theory in regard to Paget's disease is that blocked lymphatics are not the usual finding. Handley circumvents this by saying the lymphatics have been obliterated by perilymphatic fibrosis.

Muir in 1927 published the most complete work on this disease up to that time. He studied the disease when Paget's cells were in evidence, but no infiltration of the nipple by ordinary carcinoma was present, because he admitted the picture present in Paget's disease may result from carcinomatous infiltration. He describes constant changes seen in the ducts varying from simple papillomatous outgrowths with thick stroma to irregularly massed differentiated epithelial cells with large

vesicular hyperchromatic nuclei. He says it is better named intra-duct carcinoma than duct carcinoma, as it is not infiltrating the duct walls. It spreads in the deeper layers of the epithelium and down into the acini. In the epithelium it spreads in the lower layers, lifting up a superficial layer of squamous cells and pressing the basement cells into a thin layer. Periduct fibrosis may squeeze off a duct. It may start in one or several ducts and may spread from one to another. It spreads and fills the acini, but is still restrained by the fibrous membrane outside. It does not invade the dermis. Paget's cells are first seen in the rete Malpighii and are largest here, compressing and flattening the rete cells. If Paget's cells are less active they are smaller with pyknotic nuclei and may degenerate as in surface layers. No transitional forms between epithelial cells and Paget's cells were seen. Later the epidermal cells may be sloughed off and the surface formed entirely of Paget's cells. Isolated groups of Paget's cells may be seen, although all were at one time connected, showing the balance between growth and no growth, dependent on resistance and pressure of tissues, is very little. If it starts high up in the ducts, Paget's disease results, and if low down breast carcinoma results by breaking through the basement membrane into the breast tissue. The walls of the ducts in the nipple are thicker than lower down and may have a greater restraining influence.

Pautrier in 1928 gave a minute histological study of the origin of Paget's cells which corroborates Muir's theory. He studied an early case with only epidermic involvement and no lump in the breast. Some lymphocytic infiltration was seen and two milk ducts were occluded by glandular epithelioma with Paget's cells. In favour of this arising from duct and not skin were the following facts.

1. It was found around such ducts as are usually involved in carcinoma starting in this duct and not in the skin.
2. Secretory cavities were lined by cells with "Kittleisten" which are found only on cells of glandular origin.
3. In the breast was deep carcinoma of glandular origin but not clinically diagnosable.

Wainwright feels that neither the skin lesion nor the carcinoma is secondary to the other but all arise independently from causes that have affected all the places. He shows a breast with four different histological types of carcinoma present, and feels that they could not have spread from one focus or one of them would be larger than any that were found, and that it would also digress from the theory of specificity of disease. He claims that Guy's theory by which a specific substance and an infecting agent are both necessary, is the only one that will explain his section. He says some change in the breast has produced Guy's specific substance in many cells all through the breast. Then the infecting agent was introduced and several nodules started independently, each developing. its own type Cramer has said of Guy's hypothesis. "It does not conflict with any previously established facts, but confirms them. It removes all apparent controdictions. It explains all essential features of the disease."

Fraser in 1928 consulting Muir, Pautrier, and Cheatle, concludes it is not a dyskeratosis but a metastasis from duct carcinoma, but that Cheatle's view of multiple primary origin must also be considered.

Some cases called Paget's disease have been described as occuring on abdomen, buttock, genital organs, etc. Many on histological examination were really intra epithelial carcinoma. Muir says it is probably carcinoma starting in epidermis and spreading in deeper layers but not invading the dermis. (If this can happen, why is it so infrequent?). Pautrier feels the extramammary forms are dyskeratosis or carcino-

ma starting in sebaceous ducts, and not true Paget's disease.

Conclusions.

The present tendency is to adopt the conclusions of Muir and Pautrier and Fraser which have developed from the elaboration of ideas of Jacobeaus, Ribbert, Schambacher and Sekiguchi, and which are summed up below.

1. Paget's disease is not a dyskeratosis.
2. The pathognomonic feature is the Paget's cells which are virile invading cells, cancerous from the outset and of glandular origin, from the upper extremities of the lactiferous ducts affected by neoplastic disease, which invade the epidermis of the nipple and spread intraepidermally.
3. The invasion leads to reaction in the underlying connective tissue, infiltration of cells, new capiliaries, congestion, and serous exudate.
4. The disease of the ducts is intraduct carcinoma of low malignancy also spreading to acini but remaining within the duct outer lining until great proliferation has taken place, when it may break through and ordinary infiltrating carcinoma result.
5. Study of "extramammary Pagets" does not refute this theory, but corroborates it.

Treatment.

Paget recommended excision of the ulcerated area to remove it before it induced such degeneracy in the underlying tissues as to lead to carcinoma. All subsequent investigators are unanimous in recommending the radical operation for removal of the breast to remove all lymphatic and fascial areas which may have become involved.

Case Reports.

This disease is surprisingly rare as evidenced by the fact that in the Toronto General Hospital, a clinical diagnosis of Paget's disease has been made in only five cases. On Histological section only two were substantiated and these in 1922 when the knowledge of Paget's cells was not complete with the result that serial sections were not made and little is to be gained by a study of the slide presented. The cases show a picture of hyperplastic squamous epithelium, mitotic figures in pale staining, atypical cells, which do not invade the corium, which is infiltrated and with narrowed papillae. The pathologist reported no evidence of malignancy.

There is a specimen in the museum of surgical pathology of a nipple with excoriation of nipple and areola, patchy incrustation of blanched and thickened epidermis, erythematous and weeping, with deep seated carcinoma present. No section of the nipple was made.

One patient was admitted in 1922 with a clinical diagnosis of carcinoma of the nipple. A quick section was made, diagnosed chronic eczema and local excision of the nipple was done. Patient returned in 1929 with carcinoma of the breast. The pathologists reviewed their diagnosis and adhered to it.

We feel that little profit may be derived from studies of these cases and agree with Pautrier that the solution will be arrived at only by careful histological examination of serial sections from early cases.

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ARTHRITIS.

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The question of arthritis, both acute and chronic is, at the present itme, receiving a great deal of attention by the professional and lay men alike. Huge inroads each year are made upon the resources of unfortunate sufferers, and the loss in industry due to some form of this condition is surprisingly great. As a result of this loss, which has become more apparent since compensation boards and other forms of insurance, have been introduced, great strides have been made in the last decade towards its eradication; but the etiology and treatment of many forms are still a matter of doubt and of great speculation.

Many classifications will be found in the literature. The following may be satisfactory to the student and general practitioner.

I. Specific Infective Arthritis.
  (a) Suppurative.
  (b) Tuberculous.
  (c) Gonorrheal.
  (d) Syphilitic.
  (e) Typhoid.
II. Traumatic Arthritis.
III. Rheumatoid Arthritis.
IV. Osteoarthritis.
V. Metabolic Arthritis.
  (a) Gout.
  (b) Scurvy.
  (c) Haemophilia.
VI. Arthritis of Toxic Origin.
  (a) Hydrarthrosis.
  (b) Anaphylaxis.
VI. Rheumatis Fever.
VII. Rheumatic Fever.
VIII. Arthritis of Nervous Origin.

I. SPECIFIC INFECTIVE.

(a) Suppurative (Due to pyogenic organisms).

(i) Acute Suppurative Arthritis.
(ii) Pyaemic Arthritis.
(iii) Secondary to Disease of Neighbouring Joint.
(iv) Acute Arthritis of Infants.

(i) Acute Suppurative Arthritis.

Eliology. The organism chiefly responsible for this condition is staphylococcus and occasionally streptococcus. The mode of infection may be due to a bacteriaemia or due to a puncture wound carrying the organisms into the joint cavity. Due to its method of infecting, almost any joint may be infected; but it occurs more frequently

in the exposed joints and may preponderate slightly in the males. These conditions may follow a skin lesion such as a furuncle or a boil. The age and sex seem to have little importance as to the incidence of infection.

Pathology. It is a typical inflammatory reaction which goes on to the stage of suppuration and usually ends, if it does not prove fatal, by fibrosis and ankylosis. The synovial membrane becomes hyperaemic and greatly thickened and succulent from exulation into the interstices. The pearly surface becomes dull and opalescent, and is rapidly covered by fibrin shreds, being converted into granulation tissue. The synovial fluid is increased in amount by the outpouring of serum; the opalescence of the fluid soon disappears and becomes purulent, and even may be blood stained, depending upon the severity of the reaction.

If it continues, the cartilage becomes vascularized, the pearly appearance changes to a dull yellow color, and eventually ulcerates in places. The bone may give rise to granulation tissue which may strip the cartilage and cast it off into the joint cavity. The surrounding tissues are also affected; the ligaments become softened and may stretch resulting in dislocations. Likewise the bony tissues may be attacked, producing erosion of the ends, and sequestra may follow. If no drainage is provided, erosion of tissues rupture, and the point of exit may be at some distance from the primary site. The healing is by fibrosis which produces an ankylosis of the joint which may vary from a slight stiffening to a completely immobile joint. True bony ankylosis occurs oftener after the suppurating arthritis than any other joint condition.

Signs and Symptoms. This condition is characterized by (1) pain, which is increased on movement, (2) swelling, which is greatest about the affected joint, (3) fever, which may range from 102°F. to 104°F. (4) the pulse rate may be increased up to 110-120 per minute, (5) rigors frequently occur, (6) hyperaemia and oedema of the skin may occur as a later sign, and (7) prostration and toxaemia of the patient in later stages if the condition is not relieved.

Treatment. Early diagnosis and vigorous treatment are essential. The ultimate function of the joint will vary according to the time in which the destruction goes on. Incision and drainage should be made at once. A drain may be put in, down to the capsule, but not within it. Irrigations of a normal saline solution, or of Dakin's solution are of value. The joint should be fixed in a splint and slight traction, just sufficient to relieve the pressure on the cartilage gives much relief. In severe cases eradication of the joint or amputation is necessary.

(*ii*) *Pyaemic Arthritis.*

This condition is generally similar to the acute suppurative except that several joints may be affected in rapid succession. As a rule the condition is not quite so acute. Treatment is similar but has to be carried out on several joints instead of one.

(*iii*) *Secondary to Disease in Neighboring Bone.*

The primary site of disease may be an osteomyelitis which erodes into a joint and secondarily infects the joint. The condition is similar to a suppurative joint and due to its mode of production is usually associated with the long bones. Treatment consists of early drainage of the primary focus and prevention. When the joint is involved, drainage is also essential from the joint itself.

(*iv*) *Acute Arthritis of Infants.*

Etiology.—It usually occurs in children under one year of age, attacking most frequently, the knee, hip and shoulder. The infecting organisms are usually, staphylococcus, gonococcus, and pneumococcus. The blood stream carries the organism to the site from a lesion such as an infected umbilicus or from a vaginitis or conjunctivitis etc., and lodges in the epiphyses forming an

acute epiphysitis which later ruptures into the joint.

Pathology.—It is similar to any other acute purulent arthritis. It begins usually at the growing end of the diaphysis and spreads directly into the joint.

Symptoms.—The acute stage may be preceeded by local symptoms, such as a high and widely fluctuating temperature. The affected joint is flexed, painful and tender; it rapidly becomes swollen and distened with pus. Either one joint or many may be infected simultaneously.

Treatment.—Opening and drainage of the affected joint with fixation is essential for recovery of an useful joint. Some of the gonorrheal infections subside without incision and an useful joint is recovered. In other forms of infection, early drainage is essential as the condition has a high mortality rate

(b) Tuberculous Arthritis.

Etiology.—The joint may be infected directly or involved secondarily to an adjacent bone infection. If it is direct, the lesion is usually found in the synovial membrane and if secondarily, the lesion occurs in the articular end of the bone. The age incidence is greatest under 6 years of age but may be found with decreasing frequency up to old age. Tuberculosis of the joint in children usually attacks the epiphysis because of its vascularity and spreads to the joint. In adults, it is usually a direct synovial membrane lesion, later involving the joint.

The joints most commonly affected are the hip, knee, elbow, shoulder and ankle in order of frequency. The onset of the disease is very frequently preceeded by a local injury, which is sufficient for a blood borne organism to settle out and become active. There is usually a primary lesion elsewhere in the body, such as a tuberculous mediastinum or pulmonary lesion.

Pathology.—Whether the lesion is direct or secondary in the joint, the end result is nearly identical. The synovial membrane may be studded with tubercles, causing it to lose its smooth shiny surface. Its color is a dirty gray and due to a tourniquet, at operation, it may appear plum colored. The membrane is swollen, and redundant and due to this most of the swelling occures, rather than to an increase in the synovial fluid. In later stages, the membrane becomes tuberculous granulation tissue and will be studded with caseating masses.

The joint cavity may not have any increase in fluid contents, but filled with masses of synovial membrane. What fluid there is contains fibrin flakes which may be deposited on the surface of the synovial membrane, giving it a shaggy appearance, which gives rise to foreign bodies known as melon-seed bodies or joint mice.

The articular cartilage will sooner or later be involved. The disease never primarily starts in the cartilage because of its lack of vascular structure, but may be attacked from its superficial or deep structure. The commonest method of attack is for the synovial membrane to creep over its surface. At first it can be easily stripped but as it continues, it erodes and disorganizes the cartilage. The cartilage becomes opaque and yellowish and is converted slowly into granulation tissue which lays bare areas of bone. At this stage the characteristic "night cries" occur.

If the synovial membrane becomes caseous, the erosion of the articular capsule is checked from the superficial surface, but it may be attacked from below by an invading ring of vascular granulation tissue. This invading ring is composed of fibroblasts, numerous capillaries and round cells and contains no tubercles, epithelioid or giant cells. This may be a foreign body reaction to the dead cartilage, and this may go on to detachment of the articular cartilage.

If the primary joint lesion was in the bone, the bone will be well attacked by this time, but if the primary were in the membrane, at this stage, the bone is eroded by a rarefying osteitis.

The ligaments, along with the soft parts are involved and produce a softening with stretching and may be finally disorganized and destroyed, which results in pathological dislocations.

Should secondary infection occur in these joints, a true pyogenic or pus infection is bound to occur which is likely to go on to amyloid degeneration of the liver, spleen and kidneys. The time required for this to occur varies greatly, from a development in a few months, to a course of over twenty years without occurrence.

Signs and Symptoms.—Most tuberculous joints are characterized by their insidious onset, resulting in consider able invasion having been made before the condition is noticed. The cardinal symptoms and signs are: (1) lameness occurs if the lower extremity is involved, which may only be found on careful examination due to an intermittent appearance; (2) Pain, may occur early or late. The characteristic night cries are very suggestive. The pain may be referred to some distant position, such as the knee, when the hip is involved. (3) Swelling may be only elicited when carefully compared with the normal. Fluctuation may be hard to elicit, because the synovial membrane is largely responsible for the swelling in early cases. (4) Limitation of movement is produced by a protective spasm of the muscles and is one of the most constant signs. This however may disappear after the limb is at rest but usually quickly returns after exercise. (5) Muscular wasting is usually present and most marked in the most powerful group of muscles about the joint. The muscle tone is usually reduced as well. Taken alone, the sign may have little significance, but along with other signs it is of diagnostic value. (6) Deformity in early stages is due to the muscular contracture or spasm, but in the later stages may be due to actual bony deformity.

In doubtful cases, the X-ray is of great value and similarly the laboratory examination of the fluid in the joint may be of inestimable aid in diagnosis.

Treatment.—The full treatment of tuberculous arthritis is too large to include here in its full extent. Consequently the general principles will be mentioned.

It is essential to increase to the maximum the patient's general health, by good food and good hygienic surroundings. Cod liver oil, sunlight, fresh air and good food are the essentials for such treatment. The local treatment consists of correction of the deformity, fixation of the joint and some form of traction to relieve interosseous pressure. This form of treatment has to be continued over many months or even several years.

(c) Gonorrheal Arthritis.

Etiology.—Usually there is some site of gonococcal infection primarily such as a vaginitis, urethritis or conjunctivitis. The larger joints are chiefly affected and it is usually mon-articular, occuring about the third week or during the decline of the acute primary infection. Although it is difficult to find the organism, quite frequently it is isolated from the affected joint. The condition is much commoner in males, and usually occurs in adults, but it may be found in children when they have some other primary site of infection.

Pathology.—The picture of the acute and subacute forms is similar to any other acute arthritis except for more periarticular swelling as a rule. The pain is apt to be intense with rapid effusion, along with redness, oedema and constitutional disturbances. It may resolve rapidly, suppurate or develop into a chronic form. In suppurative cases, the end result may be ankylosis.

Signs and Symptoms.—The pain, acute swelling, redness and oedema with constitutional reactions indicate an acute arthritis whereas the previous history or findings of gonorrheal infection should materially aid in the diagnosis of the condition. Aspiration of the joint with the isolation of gonococcus is diagnostic.

Treatment.—The original site of infection should be vigorously treated.

The joint should be fixed after deformity has been reduced by stretching with weights. For the severe pain, morphia is necessary. After the acute stage has subsided, the reabsorption of the fluid may be assisted by message and counterirritants.

(d) Syphilitic Arthritis.

Etiology.—Joint lesions of syphilitic origin are probably commoner than once thought to be. In the Panama Canal zone, Clark performed 1,110 autopsies of which 176 had joint lesions of which 96 were due to syphilis. It involves the joints in either the congenital or acquired form. The acquired form involves the joint in either the secondary or tertiary stage.

Pathology.—The arthritis in the secondary stage is principally a soft tissue condition which is characterized by a synovitis with or without moderate degrees of swelling. One or more joints may be attacked and may be symmetrical. The knees are the common site of attack. In the early mild attacks, this condition may be analogous to the reaction in the mucous membrane to the organisms. The effusion may persist for long periods of time and be quite intractable to treatment.

In the tertiary stage, we may have a gummatous condition involving either the synovial membrane or the bone. In the synovial type, the membrane may become as much as one-half an inch to one inch in thickness, this produces a marked swelling of the joint and to the naked eye, closely resembles tubersulosis. There may also be gummatous erosion of the bone cartilage. In the osseous form, the ends of the bones are firstly involved which spreads to the cartilage and synovial membrane.

Signs and symptoms.—The outstanding feature of this condition is the swelling which may have little or no pain and little limitation of movement. It is necessary to differentiate between sarcoma and syphilis. This is frequently difficult to do. In order to arrive at a diagnosis, the history, Wasserman reaction, evidences of infection, must all be taken into consideration.

Treatment.—Generally the condition should be treated with anti-syphilitic measures. Locally, the deformity should be reduced, and rest be obtained by splinting the joint affected. Some of the congenital forms are extremely resistant to treatment.

(e) Typhoid Arthritis.

Etiology.—Usually occuring towards the end of the disease and most frequently monarticular, attacking usually the hip joint. Typhoid organisms are usually found in the pus.

Pathology.—The condition may remain a serous reaction or go on to pus production. The cavity is distended with fluid or pus and the joints offected are stretched allowing a backward displacement in the hip joint Healing may give a freely movable joint or ankylosis.

Signs and symptoms.—The signs are those of an acute condition coming on towards the end of the course of typhoid fever.

Treatment.—Aspiration of the joint and fixation so that backward displacement will be prevented.

II. TRAUMATIC ARTHRITIS.

This is sometimes known as a simple synovitis.

Etiology.—The precipitating cause is a sprain, dislocation or contusion of the joint.

Pathology.—The injury sets up a local hyperaemia and congestion which is localized to the synovial membrane. The synovial fluid is increased in quantity, which may be clear or blood stained depending upon the severity of the trauma. Due to the absence of fribrin in the fluid, rest will soon lead to its absorption and no permanent disability results.

Signs and Symptoms.—There is (1) an early swelling due to effusion. (2) pain and tenderness, and (3) heat. Due to the swelling of the joint, the limb will show some impairment of movement and likely some muscle spasm.

The condition must be differentiated from periarticular injury, inflammation of the neighboring bursae and tendon sheaths, fractures of the bones, and ruptures of tendons and ligaments.

Treatment.—The joint should be put at rest in a splint. An ice bag or hot fomentations hasten the absorption of the fluid. Aspiration of the joint may be necessary if greatly distended. As soon as recession begins massage should be practised. Movement of the limb should be gradually encouraged. Baking in hot air or radiant heat may be of considerable value.

III. RHEUMATOID ARTHRITIS.

Rheumatoid arthritis receives many other names of which the commoner are chronic infective arthritis, proliferative arthritis, synovial type of chronic arthritis and others. Almost each writer has a different method of classification and nomenclature.

Etiology.—This condition is found most frequently in females between the ages of twenty and forty years. It is not uncommon in children but to a lesser degree.

As soon as the cause of rheumatoid arthritis is suggested, numerous difficulties are encountered and many theories have been discussed. A few of these theories will be mentioned.

The infective theory has been the centre of a great deal of attention. Infection may play a role either as an invasion of the joint, or secondarily to some condition elsewhere in the body. For the first conception, it can be said that many investigators have reported finding organisms in the joint, and isolating them. Recently Cecil has reported finding a low grade hemolytic streptococcus in 60% of his cases. Other investigators have found other organisms. The results tend to shake ones confidence in the results as the same investigator finds organisms in a relatively low number of cases and different men find varying organisms. One is forced to wonder if errors in technique or contamination does not play some part in their findings. On the other hand, the role of foci of infection in the body other than the joint itself is building up a formidable array of evidence.

Some of the evidence in support of the foci of infection theory is a follows: When rheumatoid arthritis occurs in a child, there is frequently associated with it, enlargement of the spleen and lymph glands and some constitutional reactions. Many cases are on record of remarkable recovery when some foci such as teeth, tonsils, sinuses, etc., are definitely removed. This evidence is sufficiently striking that it cannot be ignored.

Boyd states that the evidence is overwhelmingly in favour of the infective theory, i.e. that there is some site or sites of infection in the body, because of

1. That many of the patients are pale and in an unhealthy state, suffering from malaise, irregular attacks of pyrexia, palpitation and sweating, and in short, their whole appearance suggests a toxic condition.
2. The undeniable evidence that these cases make a spectacular recovery when the foci of infection, such as are found in the teeth, tonsils, etc. are removed.
3. Measures such as producing a protein shock, which are directed against the infection, have a most beneficial effect upon some people.

It is also reported by Arbuthnot Lane, that great benefit has been obtained by doing colectomies with the idea or removing colons which are absorbing toxins or perhaps are foci of infections themselves. Such procedures, although drastic have been followed by very good results in many cases.

Recently in Toronto General Hospital, Fletcher has been able to demonstrate in two thirds of the chronic arthritics, that an abnormal condition of the colon prevails, consisting of an atonic condition, in which the haustral markings are lost and great looping of the bowel is present due to increased length. It has also been demonstrated that this is a pre-arthritic condition as

well. These patients have done exceedingly well when their diet has been changed so as to correct this condition. Malnutrition is an important factor and from experience it has been found that a diet with high vitamin B content and low in carbohydrate soon changes the radiological picture. The size of the colon in length and diameter is reduced and the haustral markings return, in short the normal picture is resumed. Along with the return to normal of the bowel, the joint conditions frequently show marked improvement. This may be one other means of getting rid of a definite foci of infection, which may be a precipitating or causal factor.

As opposed to the infective or foci of infection theory, the older ones of environment enter in. Exposure to cold, dampness, fatigue as predisposing factors have some supporters. In industrial cases fatigue may be an important factor. Metabolic and endocrine disturbances have received their share of blame for this condition, and in some cases seemingly rightly so. Pemberton has been in favour of the cause being due to faulty diet and nutrition.

Just recently the American Committee for the Control of Rheumatism expressed the view that chronic arthritis is a general disease with joint manifestations.

In a summary, it can be said that at present, the etiology of rheumatoid arthritis is unknown, but evidence is accumulating which suggests that bacterial infection probably in the role of foci of infection is the one most important factor in its causation.

Pathology.—The joints chiefly affected are the small joints, especially the proximal interphalangeal and metacarpophalangeal joints. In addition, the wrist, shoulder, knee, and temporomandibular joints may be involved.

Essentially the condition is one which attacks the synovial membrane and might consequently be termed a synovioarthritis. The condition may never spread beyond the membrane. The membrane is greatly thickened, due to proliferation which forms pulpy masses or fringes or numerous tags. An increased production of synovial fluid contributes greatly to the size of the joint.

If the condition progresses, the synovial membrane begins to encroach upon the articular surface of the cartilage, This is known as pannus formation and beneath this the cartilage is ulcerated and eroded. Adhensions tend to form between the pannus formations and whether this is fibrous, cartilaginous or osseous determines the degree of ankylosis of the joint. In time the entire joint may be involved by such a process. In addition to the eroding action of the pannus, granulation tissue may be formed from the epiphysis due to irritation, and the process of erosion is continued on the deep surface of the cartilage. Osteoblasts may also lay down new bony formations on each side of the cartilage. In time the ligaments become softened, and absorbed due to the periarticular reaction. Fibrositis adds materially to deformity, which is increased by muscle spasm and continues slowly to a terrible deformity if not checked.

Signs and Symptoms.—The onset of rheumatoid arthritis may be very acute and suggest acute rheumatic fever. The joints are swollen, tender and hot to the touch but not particularly red. Pain is apt to be intense and increased on movement. This condition persists for some time, perhaps several weeks and in the later stages deformity is evident, even subluxation may occur. On the other hand, the condition may develop insidiously having a very slow onset. If prompt treatment is employed it may resolve early. If resolution fails to take place, the course is one becoming progressively worse. The swelling of the joint feels doughy and no deformity until late is palpable.

Treatment.—Naturally where the etiology is doubtful and the results so poor, many forms of treatment are found. The search for and complete eradication of foci of infection seem to be very important. Fletcher working on his patients has found that malnut-

trition predisposes to chronic arthritis and may be due to a condition of the colon which leads and assists in greater absorption from the bowel of toxins or bacteria. With this in mind, general improvement in nutrition and in the health of the patient is desired. Vitamin B is given in the form of fresh baker's yeast one cake three times a day before meals, provided flatulence or distension does not occur in which event it is reduced. The extract of yeast, marmite, may be better borne. One half ounce of wheat germ may be added to each meal, preferably uncooked and taken in milk or mixed with other food. The diet should be readjusted so that between 50 and 100 grams of carbohydrate are given daily. If the patient is underweight, he should be given a high calorie diet, and if overweight, the calories should be slightly below requirements, other problems enter in, such as intolerance to high protein content, manifested by putrefaction; in such cases milk and buttermilk should be the chief sources of protein.

Locally, the important thing is to prevent deformity, so a splint should be applied to put the joint at complete rest. Other things of value, are radiant heat, baking and massage after the acute stage. The pain may be relieved by drugs such as acetyl salicylic acid, neoincophen, iodides and arsenic.

IV. OSTEOARTHRITIS.

Osteoarthritis is also known as hypertrophic arthritis, or degenerative arthritis.

Etiology.—This disease commonly occurs in people who have reached middle or old age, and is much more common in women than in men, with the exception of young people, and then it is more common in men.

The causative factor is unknown. On reading the various causes suggested, it would be fair to conclude that any factor which tends to reduce the blood supply or nutrition of the joint is a contributing or precipitating cause. Those commonly mentioned are exposure to cold and dampness, trauma or chronic irritation, an abnormal strain such as in genuvalgum, a previous infection such as a gonorrheal arthritis, changes in internal sections as may occur in women at the menopause, old age which may be due to a change of the vessel walls as osteoarthritis not uncommonly occurs with arteriosclerosis and an obliterative endarteritis.

Usually fewer joints are affected than in rheumatoid arthritis, and quite often it is confined to one large joint. The most commonly affected joints are those of the hand and feet, although the hip, knee and shoulder are frequently involved.

Pathology.—As the name signifies, it is principally a process involving the bone, starting first in the articular cartilage, later involving the bone and still later the synovial membrane. The smooth surface of the cartilage becomes roughened, resembling velvet, by a peculiar rearrangement of the direction of the cartilage cells. They become arranged in columns at right angles to the joint surface with a separating matrix, which degenerates into fine fibrillae running in the direction of the cartilage cells. The cartilage cells increase in size, become distended and rupture the capsule, discharging into the joint cavity. The cells give the fluid its opalescent appearance and the remaining matrix produces the velvety appearance of the cartilage surface. The opposite articular surface wears it down unevenly which leads to a heaping up of one cartilage to fit with the erosions of the other surface in the hinge joints. This process occurs first in the cartilage and then is carried on into the bone. In the ball and socket joint, since the axis of movement is in many directions, this does not occur.

The process at the periphery is different because of some factor which may be an increased blood supply. The cartilage cells proliferate in excess of their destruction which leads to a heaping up of cells, forming a series of exchondroses, which occur as a ring around the margin, producing an appearance of lipping. The cells which

produce the lipping are largely of the synovial perichondrium. Many of these chondrophytes become ossified and converted into osteophytes whose surface eventually degenerates and the subjacent bone becomes eburnated. These new formations in many cases actually increase the joint surface, and supporting bone structures are evolved to support and strengthen the ring of osteophytes. Sections of the ring may become dislodged acting as a foreign body within the joint cavity.

As the cartilage is gradually eroded, the surface of the bone is exposed, and eburnated, which is a process of hardening and polishing giving a resemblance to ivory. The bone which is deep to the condensed layer undergoes a slow process of rarefaction and absorption. Simultaneously new bone formations may occur at the margin, giving excrescences and producing a mushroom like appearance.

If the process continues long enough to involve the synovial membrane, it becomes thickened and shaggy and a series of tags or fringes are formed, hanging into the joint cavity.

The synovial fluid is only slightly increased early and is milky as described, due to the presence of the discharged cartilage. The ligaments are softened and seem to melt away, which allows deformities up to dislocation. Tendons may share a similar fate.

Heberden's nodes occur in this condition and are small bony outgrowths on the sides of the distal phalanges at the terminal phalangeal joints.

Boyd gives the following comparison between rheumatoid arthritis and osteoarthritis.

Chronic Infective Arthritis.	**Osteo-Arthritis.**
A disease of early adult life.	A disease of over middle life.
Symptoms of constitutional disease, suggesting infection.	None.
Synovial membrane and periarticular tissues chiefly affected.	Cartilage and bone chiefly affected.
May be acute in onset and run a rapid course.	Essentially chronic.
Hip joint rarely affected	Hip joint often affected.
Effusion into the joint common.	Effusion into the joint rare.
Fibrous adhesions between articular surfaces.	Any rigidity due to bony outgrowths around joint.
No Heberden's nodes.	Heberden's nodes may be present.
Many joints involved, usually in a symmetrical manner.	Often only one joint affected; usually symmetrical when multiple.
No relation to previous injury or disease of the joint.	Previous injury or disease frequent.

Signs and Symptoms.—Usually the patient complains of a painful and creaking joint. The pain is not constant, and stiffness is also present. Pain and stiffness may vary with use, mild exertion relieving the condition and violent exercise bringing it out more acutely. The creaking may be felt on examination of the joint. The lipping of the osteophytes can be frequently felt. Muscular wasting and muscle spasm are far less striking than in rheumatoid arthritis.

The onset is slow and insidious and not associated with symptoms of toxic absorption. If there is any deformity it is usually due to alterations in the shapes of the bones. When it occurs in the hands, the knuckles are like knobs the distal phalanges are enlarged and the intervening phalanges are free from disease. There is also a characteristic ulnar deviation of the fingers. True ankylosis does not occur and any limitation in movement is due to bony outgrowths around the joint.

Treatment.—If treatment is to be of any value, it must be carried out before the disease process has progressed very far. Due to the possible variety of causes, treatment has been unsatisfactory. Foci of infection are removed, hoping to check the condition. Middle-aged women who are gaining weight are sometimes relieved by thyroid extract and a reduced carbohydrate intake. It is desirable not to put the joint at rest unless the pain is too severe. Massage to increase blood flow, douching, vapour baths, radiant heat and hot air baths, all seem to have a

measure of success in certain cases. If the painful condition does not yield to any form of treatment, it may be necessary to perform an operation and do an ankylosis.

V. METABOLIC ARTHRITIS.

(a) **Gout.** A disorder of metabolism associated with retention of uric acid and of other purin bodies in the body, characterized clinically by attacks of acute arthritis, the deposition of sodium urate in and about the joints, and by occurrence of irregular constitutional symptoms. (Osler).

Etiology.—All the mammals with the exception of man, apparently have the power of converting uric acid into the more easily soluble substance allantoin. Since man has not this power, gout is a disease produced by faulty elimination rather than imperfect oxidation.

The normal daily output of uric acid is between 0.4 gms. and 1.5 gms. The amount excreted is increased in the day time and is also increased by diets high in purin bodies, also by exercise, fevers and exposure to cold. As a rule in gouty persons the amount eliminated is low.

There are several predisposing factors, such as:

(1) Heredity. In from 50 to 75% of cases, there is a hereditary history which is most commonly transmitted on the male side.
(2) Alcohol. The consumption of large quantities of alcohol, particularly beer and malt liquors, is a factor.
(3) Food. High purin content of food and a sedentary life with rich foods, are predisposing factors.
(4) Occupation. It is not uncommon in very active people. It also occurs commonly in those occupied in the manufacture and distribution of alcoholic beverages.

An exciting cause, such as an excessive meal with alcohol, mental shock or worry, or in sensitive individuals a slight injury is enough to precipitate an attack.

Pathology.—Adler and Ragle found that normal uric acid was 1.7 mgms. per 100 c.c. of blood with a range of 0.7 to 4.5 mgms. Pratt showed in 21 cases of gout that the uric acid content was 3.7 mgms. per 100 c.c. This excess is greater during attacks than during the intervals and is also found to be increased in leukaemia and in severe nephritis.

Various joints are involved, but the order of frequency is the great toe, ankle, knee and small joints of hands and wrists. There may be deposits in all the lower joints and none in the uppers.

The first change is in the cartilage and other regions where the circulation is rather inferior and is a local necrosis. The articular cartilages are first involved, with a gouty deposit of sodium urate uniformly distributed or in small patchy areas. The deposit is invariably interstitial covered by a thin lamina of cartilage, appearing superficially and thickest at the part most distant from active circulation. As well as the cartilage, the ligaments and fibrocartilage ultimately become involved by the urate deposits forming the so-called chalk stones or tophi. Skin usually covers the tophi, but occasionally this ulcerates and the chalk stones are visible. There may be in advanced cases immobility due to excessive deposits and also some true exostoses may be formed. Cartilage in the nose, ears, larynx and eyelids may have tophi appear.

Important renal and vascular changes are apt to be associated with gout such as (1) urate deposits in the renal pelvis in the region of the papillae, or interstitial deposits of urates in the medulla and cortex; (2) interstitial nephritis; (3) or arteriosclerosis and cardiac hypertrophy.

Signs and Symptoms.—Premonitory signs such as twinges of pain in the small joints of the hands or feet, nocturnal restlessness, irritability of tem-

per and dyspepsia are common. The urine is scanty, high coloured and a transient albuminuria may occur which is preceded by a low output of uric acid which is rapidly rising. The attack characteristically occurs in the early morning hours and subsides for the rest of the day. The pain is agonizing, usually starting in the metatarsophalangeal joint. Sydenham says of it, "insinuates itself with the most exquisite cruelty among the numerous small bones of the tarsus and metatarsus, in the ligaments of which it is lurking."

The joint is swollen, hot, tense and shiny, but does not suppurate. There is some fever, up to perhaps 102 to 103 degrees F. The acute attacks last usually about five or eight days and a moderate leucocytosis may prevail. In addition to the above a careful history of the patient's habits of living and hygiene may give valuable aid in making the diagnosis.

Chronic gout may occur in which the onset is much more insidious, not resembling the above picture in severity. Tophi become marked and the condition lasts in its painful stage much longer. General systematic changes are noted in the chronic condition such as dyspepsia and frequently arteriosclerosis.

Note: The remainder of this article on "Arthritis" will be published in the May issue of the Journal.

Short Synopsis of The History of Anaesthesia.

By MARGARET K. PATTERSON, 3T0.

The artificial induction of anaesthesia has come to occupy a foremost place in modern medicine, but there is abundant evidence to show that it is a practice of great antiquity.

Homer, in the "Odessey" says: "Helen dropped into the wine of which (the soldiers) drank a drug, an antidote of grief and pain, inducing oblivion to all ills." The sedative draught used at this time is believed to have been nephenthes, a deodorized opium preparation. In Egypt, cannabis indica, the modern hasbish which is smoked by the Arabians of the present day, was burned and its fumes inhaled to alleviate pain.

From an old Chinese manuscript, it appears that a physician named Hoatho, who lived in the third century gave his patients a preparation of hemp, which rendered them insensible during the performance of surgical operations.

The Romans used memphis marble as a local analgesic; this was finely powdered and applied to the part and on the addition of vinegar, a gas, carbon dioxide, was given off which it is said rendered the part slightly anaesthetic.

Various members of the Euphorhiaceae, Mandragora and other Solonaceous plants were employed in infusions, which on being drunk induced some narcotism. As early as 2000 B.C. the Babylonians used Mandragora, which in the thirteenth century was used in what were called "Drowsy syrups." Again in the sixteenth century, the soporific effects of mandrake are alluded to by Shakespeare, who also makes frequent mention of anaesthetizing draughts the composition of which is not specified.

A departure in an entirely new direction was made by Mesmer, 1734, and his followers, who averred that patients could be surgically treated without pain or inconvenience if thrown into the

"magnetic state," that is hypnotised. In 1829 Cloquet amputated a breast, the patient having been rendered insensible by having been thrown into the hypnotic state. Dr. Esdaile of India performed no less than three hundred operations upon patients in whom anaesthesia had been produced by this means. But it was found that only a certain number of persons could be completely hypnotised and even this required many seances before the requisite degree of insensibility to pain was obtained. Then too, the mental state produced in these cases was highly prejudical to physical and moral well-being and so the consensus of opinion was adverse to the employment of hypnotism.

Many and varied were the ways of producing anaesthesia before the time of Wells. In the sixteenth and seventeenth centuries, Valverdi and others operated upon patients stupefied by compression of the carotid arteries, so depriving the brain of blood. James Moore, an English surgeon in 1784 compressed the nerve trunks before cutting the areas supplied by them and John Hunter, after firmly compressing the crural and sciatic nerves of the limb, amputated a leg. Wardrop, 1832, proposed to operate upon patients rendered unconscious by bleeding them to syncope. Richmond and other surgeons adopted the plan of rendering their patients intoxicated before applying the knife.

Towards the close of the eighteenth century the discoveries of Priestley gave an impetus to chemical research and the properties of gases and vapours began to be more closely investigated. In 1800 Sir Humphrey Davy discovered the anaesthetic properties of nitrous oxide. He suggested its employment in surgery but his suggestion remained unheeded for nearly half a century. Faraday, 1818, showed that the inhalation of vapour of ether produced anaesthetic effects similar to those of nitrous oxide. But these observations were regarded as mere scientific curiosities till December 1844 when Dr. Horace Wells, a dentist of Hartford, Connecticut,had a tooth extracted while rendered insensible by nitrous oxide. Dr Wells then proposed to establish the practice of painless dentistry, but in consequence of an unfortunate failure in an experiment at Boston, he abandoned the project.

On September 30, 1846, Dr. W. T. G. Morton, a dentist of Boston, employed the vapour of ether to produce general anaesthesia in a case of tooth extraction, and thereafter administered it, in cases requiring surgical operation, with complete success. The practice soon became general both in Great Britain and on the continent.

It was not until 1849 that Dr. Crawford Lang of Jefferson, Jackson County, published a statement that seven years previously he had administered ether to a patient and while thus nar-

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cotised, a small tumor was painlessly removed. Lang, being a busy man and of a retiring disposition postponed publishing his cases until he was forced into doing so by the claims of monopoly advanced by Morton. There can be no doubt that to Lang is rightly due the title of being the first man who actually employed ether in surgery and proved its value and safety.

Sir James Simpson was the first to use ether to abolish the pains of labour. He found that this did not interfere with the uterine contractions or injure the child in any way. In November 1847, Simpson announced his discovery of the anaesthetic properties of chloroform, the trial of which had been suggested to him by Waldie, achemist at Liverpool.

For some time chloroform was used widely in place of ether, though it was found, by several casualties, that it was not an absolutely safe anaesthetic. John Snow then commenced researches upon the subject and found that there was an optimism value for safety; this being two per cent by volume.

During the intervening period, as the results of labours of John Snow, Sir Benjamin Ward Richardson, Thomas Nunnely and Colton amongst others, several drugs were found to possess anaesthetic properties. Of these, one, ethyl chloride, which was given up for some years, was revived and used very successfully till the summer of the year 1929, when several deaths in the city of Toronto were attributed to its use. Nitrous oxide, which had been lost sight of since Well's failure at Boston, was reintroduced and it became and has remained the most popular anaesthetic in dental surgery.

In the last fifty years the science of anaesthesis has steadily advanced until now a death, attributable to the anaesthetic, is indeed a rare occurrence.

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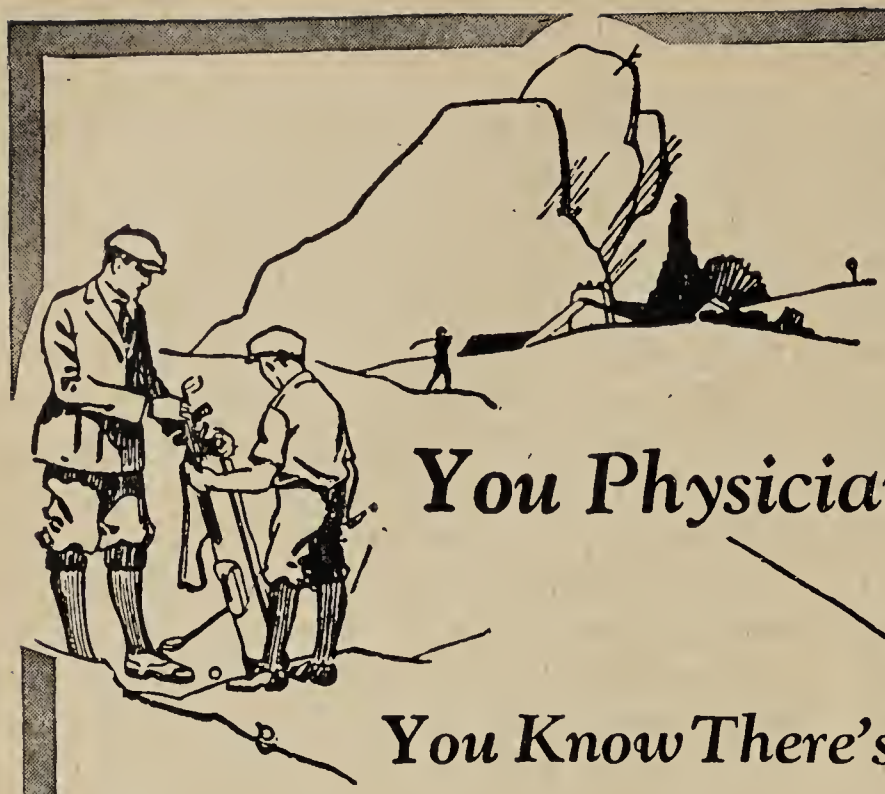

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In fact, you probably have that wonderful girl picked out already. Getting married costs money. And, of course, you'll need a car. You'll also require considerable money, from time to time, for equipment. And before you know it, you'll have a family around you — for doctors are champion family raisers — and you'll have to lay up money for the youngsters' education. All in all, you must get in a lot of money, all the time.

So take our advice — "Be Businesslike!"

Right from the start, collect your accounts promptly. Some patients may ignore your monthly statements; but remember that as long as they owe you money they will "steer clear of you." In that way, you lose practice. So turn all those slightly past-due accounts over to The Medical Audit Association, who will bring you in the money quickly and courteously — and in doing so will actually *increase your practice.*

You have no past-due accounts at present, of course. But we want you to know that we'll be here to help you when the time comes. In the meantime, here's the best of luck to you in your exams!

THE MEDICAL AUDIT ASSOCIATION

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